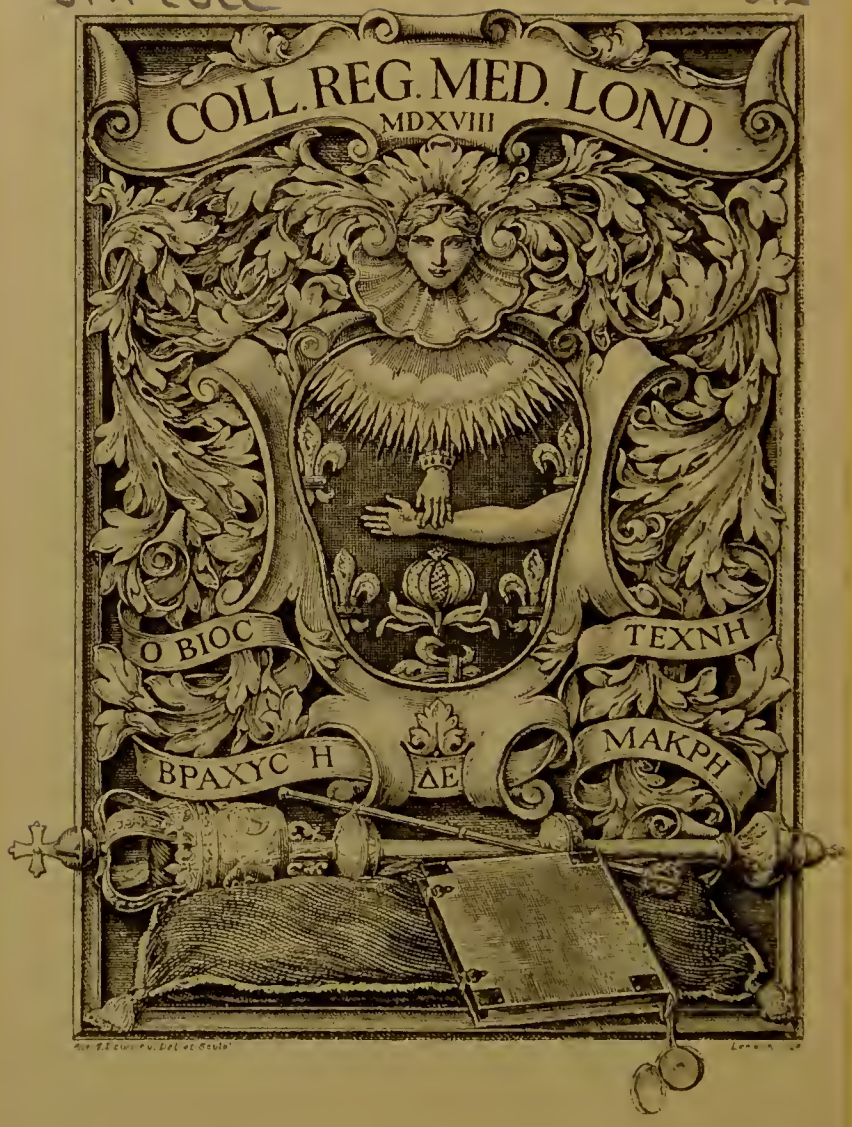

SOME DISORDERS OF THE CEREBRAL CIRCULATION AND THEIR CLINICAL MANIFESTATIONS.

BY

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SOME DISORDERS OF THE CEREBRAL CIRCULATION AND THEIR CLINICAL MANIFESTATIONS.*

LECTURE I.

Mr. President and Gentlemen,—I have first to express my deep sense of the great honour that has been conferred upon me in appointing me to deliver the Goulstonian Lectures. When I look at the names of previous Goulstonian Lecturers I see among them those of so many distinguished physicians that I am only too sensible of the great responsibility incurred by anyone whose name is to be added to that list.

The Goulstonian Lecturer was intended to devote himself to the pathological aspect of some department of medicine. My lectures will be concerned with certain pathological changes in the cerebral circulation and with their clinical manifestations.

I will begin with diminution of the blood supply to the brain as exemplified in the ordinary fainting fit.

* The 'Goulstonian Lectures,' delivered before the Royal College of Physicians, 1909.

Diminution of the Blood Supply to the Brain.

Syncopal Attacks.

The fundamental factor in the pathology of a fainting fit is a diminution in the volume of blood passing through the brain. Sir William Gowers suggests that the resulting diminution of intra-cranial pressure may be an important factor in the loss of consciousness. The causes of an attack of fainting are numerous. It may depend on cardiac disease; it is fairly common, as would be expected, in cases of severe chlorosis and in other forms of anæmia, with severe hæmorrhage, in conditions of exhaustion from whatever cause. We are concerned here, however, with syncopal attacks occurring apart from gross disease. Such may be precipitated by very different causes, sudden shock or excitement, the sight of a street accident, the sight of blood, a hot room, hunger and so on. Many people are very prone to such attacks, and this tendency to faint on slight provocation is apt to run in families.

Physiologically two important factors are concerned: firstly, vaso-dilatation in the splanchnic area, and secondly, cardiac inhibition. It is probable that in some cases only one of these factors is primarily concerned; in others both may be involved.

The ordinary faint is usually regarded as being a very trivial matter, so that little attention is paid to

the symptoms, which are, nevertheless, of great interest. Mitchell Bruce* has epitomised them as follows :

(1) *A period preceding loss of consciousness.*—Subjective sensations are present ; a feeling of sinking in the epigastrium, of giddiness ; vision may be impaired ; hearing is usually impaired or tinnitus is present ; mentally there is a rapid fading of sensory impression.

The patient turns pale, leans against any support, eyelids tremble or close ; the pulse fails, becoming weak, small and rapid ; in other cases slow and irregular ; vomiting may occur.

(2) *A condition characterised by insensibility.*—The muscles are relaxed, the patient falls, consciousness is completely lost, the surface is pale and possibly cold and clammy. The eyes are closed and the pupils dilated ; the pulse and heart-sounds are nearly or quite imperceptible ; respiration is indistinguishable or occurs as occasional weak sighs.

(3) *A period of recovery.*—Consciousness returns gradually, the pulse improves, the senses of sight and hearing can be excited, colour returns and intelligence is restored.

Some people never faint in the whole of their lives ; in others one isolated attack occurs ; others are very prone to it on slight provocation. The emotions, such as anger, fear, joy, sorrow and

* 'Quain's Dictionary of Medicine,' art., "Syncope," 1894, vol. ii, p. 963.

horror, are among the active excitants of an attack. It is immaterial in this connection whether the mental feeling of the emotion precedes and causes the organic changes above noted, or whether the mental feeling follows on and is the result of them. Mott* has discussed this in his lectures on the "Physiology of the Emotions." The failure of the circulation is unquestionably the cause of most of the *clinical* manifestations.

Whether this sensitiveness of the cardio-vascular apparatus is due to inherent weakness in its sympathetic innervation or whether it is secondary to instability in some higher level of the nervous system is in the present connection immaterial. It is certain that many people display an instability of the vaso-motor system apart from any emotional state, although emotional disturbance may be, and often is, very evident.

S. Solis Cohen has studied this question.† He proposed the term "*vaso-motor ataxia*" for a "condition of instability of the mechanism of circulation present in certain persons, and characterised by abnormal readiness of disturbance with tardiness of restoration of the equilibrium of the cardio-vascular apparatus. The manifestations are most strikingly displayed by the heart and by the peripheral vessels of the extremities, but analogy indicates the occurrence of similar phenomena in the vessels of

* 'Brit. Med. Journ.,' April 4th and 11th, 1908.

† "Vaso-motor Ataxia," 'Amer. Journ. Med. Sci.,' 1894, vol. cvii, p. 130.

the glands and of the viscera, more especially in those of the kidney, of the gastro-intestinal tract, and of the brain. They may occur apparently spontaneously, but often there is a recognisable exciting cause. Among the influences acting as excitants are temperature, especially cold; toxic agents formed in the body, or introduced from without; visceral or internal reflex excitation; and emotion."

The vascular phenomena include functional heart disturbances, vaso-dilatation and vaso-constriction. Morbid alterations in the thyroid are not uncommon. He regards dermographism as an essential feature of the condition, and claims the existence of a hæmorrhagic tendency as shown by ecchymoses, petechiæ, epistaxis, hæmoptysis, hæmatemesis, hæmaturia, and retinal hæmorrhage. He enumerates a very large number of allied morbid associations, and among them hysteria, urticaria, local œdema, asthma, vertigo, migraine, epilepsy, neurasthenia, neurotic dyspepsia, membranous enteritis, etc.

Doubtless many would hesitate to accept Solis Cohen's scheme in its entirety, but it does gather together a series of conditions, many of which are not infrequently found in combination. All are familiar with cases presenting irregular circulatory manifestations, such as blue hands, cold extremities, chilblains, palpitation, flushings, etc., often associated with migraine, neurasthenia, dyspepsia, and so forth. Such individuals are rarely robust, and in

many of them, moreover, there is a marked tendency to faint on slight provocation. Solis Cohen does not include this in his large list of clinical manifestations, but vaso-motor and cardiac instability are very prominent features in many people of fainting tendencies. Their vascular mechanism is often unable to adjust itself to the slightest strain, as seen in the momentary faintness on getting up from a stooping position. The maintenance of adequate splanchnic control is a vital factor for health.

A sudden depression of the normal vaso-motor tone in the splanchnic area leads to a rapid accumulation of blood in the capacious vessels of that region. If only momentary in duration the result is merely the sudden sinking at the pit of the stomach—so common after any unexpected noise or fright. If of longer duration this preliminary sensation or aura is succeeded by a faint. The rapidity of onset of a faint depends on the nature of the cause, and is proportional to the rapidity with which the vaso-motor control of the splanchnic area is lost. Fatigue or a hot room is often associated with a very gradual development of an attack, and doubtless with a slowly increasing splanchnic change. The removal of the cause will often cut short the attack before unconsciousness supervenes. A sudden shock, however, may cause almost sudden unconsciousness, and doubtless very sudden splanchnic vaso-dilatation can occur. It is difficult to judge as to the degree

and frequency with which the heart may be affected independent of the change in the splanchnic area. The feeble pulse is scarcely a criterion to go by, as it must be affected as the result of the fall in blood-pressure due to the abdominal vaso-dilatation and of the small volume of blood available for the systemic circulation. It would seem probable, however, that in some cases direct cardiac inhibition does occur. The two factors might also be brought into action simultaneously.

Attacks characterised by Cardiac and Vaso-Motor Symptoms with Modification rather than Loss of Consciousness.

Attention has been drawn of late to a type of attack in which vagal and vaso-motor symptoms are prominent and in which consciousness, though modified, is not of necessity lost.

Gowers describes a series of such cases under the title of "vagal and vaso-vagal attacks."* The vagal symptoms were chiefly sensations referred to the stomach, the respiratory system and the heart. The epigastric sensations were those of oppression, or of fulness, or were indescribable. The onset of the attacks was sudden. They were never really brief, seldom lasting less than ten minutes, more often lasting for half an hour or more. A peculiar slight mental state was common; it was generally

* 'The Borderland of Epilepsy,' p. 18, *et seq.*

described as a difficulty or slowness of mental operations, a difficulty in thinking or in concentrating attention. These also always began suddenly. A sense of sudden fatigue was a common initial symptom. The vaso-motor symptoms sometimes attained a high degree, coldness of skin was common, and the pulse became small at the same time. Pallor of face and shivering were common, and sometimes amounted to a definite rigor. With the coldness of the extremities tingling and numbness in them were often described, and sometimes slight tetanoid spasm occurred. Migraine was not uncommon in these cases.

In one case of a woman, æt. 28 years, the attack began with headache and inability to fix attention, followed by sleepiness. Then ensued a feeling of intense fear, extreme coldness of hands and feet and inability to move; then an indescribable epigastric sensation, and after a few minutes violent beating of the heart with a feeling of suffocation. The attack subsided as a flush developed with a feeling of warmth, perspiration and a rigor. A curious sense of unreality in all she saw was present during the attack. In severe attacks the violent action of the heart was preceded by a feeling that it had stopped.

In another case, a man, æt. 30 years, had suffered from attacks for twelve years. Quite suddenly a dreamy mental state would occur. This was not momentary, as in epilepsy, but

persisted. With it, or just after its commencement, his hands and feet became cold, his face increasingly pale, and muscular weakness was so extreme that if he tried to sit up he fell back at once. His extremities became icily cold, even to an observer; his pulse became smaller and smaller until hardly perceptible. Consciousness was retained throughout, and he felt as if dying. This state lasted half an hour, and then he became aware that his mental state was improving, and that his feet were a little less cold. Within two or three minutes a distinct rigor set in lasting a couple of minutes, and coincident with gradually increasing warmth. He continued pale for the rest of the day. A few minutes after the rigor an urgent need for micturition was felt, and went on during the rest of the day, a large quantity of limpid urine being passed.

These symptoms may, I think, be interpreted as follows: An initial widespread cutaneous vaso-constriction is obvious. The dreamy mental state might result either from cerebral vaso-motor spasm or from a passive cerebral anæmia dependent on splanchnic vaso-dilatation. Gowers suggests that the muscular enfeeblement might be due to cerebral vaso-constriction, but it might also be aided by a vaso-constriction of the muscular area. The bulk of the blood doubtless found its way into the splanchnic area, as is suggested by the copious diuresis which occurred, and by the extreme feebleness of the pulse. The condition of the pulse

further suggests that the sum total of the blood-pressure was a marked lowering, despite the cutaneous vaso-constriction, which would tend to produce a rise of blood-pressure.

In another case a woman was subject to attacks in which a sudden sense of fatigue was followed by yawning, several times repeated, and then loss of consciousness for a second or two, after which she was well—*petit mal* in fact. But she did not always thus lose consciousness; sometimes the yawning was followed by a sense of suffocation and cardiac distress, and she felt that unless she kept perfectly still she would faint. The sense of suffocation would continue for one or even two hours, but at any moment might be ended by a moment's loss of consciousness. Gowers points out that the brief attacks were clearly epileptic, but that in the longer ones prolonged vagal symptoms (respiratory and cardiac distress) were interposed "as if symptoms usually momentary as the aura of epilepsy became protracted, extended, as it were, into a vagal attack."

In another case a woman, æt. 35 years, had attacks in which a sudden intense sense of suffocation with a feeling of tightness in the head, was followed after a minute or so by a moment's complete loss of consciousness. On its return she felt cold, first and foremost in her extremities. The coldness was so intense that it made her shiver. After about ten minutes she burst into perspiration, and simultaneously her heart began

to beat violently and the symptoms slowly subsided.

In this case the loss of consciousness was interposed between the initial symptoms and the vasomotor symptoms.

I have seen four cases which may be included under the same category.

In the first case, a man, æt. 36 years, is waked up from sleep with either a violent and rapid action of the heart or a very feeble action; his extremities go icy cold; there is a sensation of tingling and tightening of the skin of trunk and extremities with free perspiration. He turns very pale, feels faint and sometimes as if dying, but never loses consciousness. With return of warmth the symptoms subside. By vigorous movements and rubbing he has sometimes arrested the course of the attack. These attacks are not uncommonly preceded by a pleasant dream. As a boy he was very liable to faint, and this tendency was noticeable in his father, brother, and two sisters. The blood-pressure varied from 110–130, but no opportunity offered of taking it in an attack. Marked constipation was present in this case, and the relief of this with a rest-cure caused an almost complete cure. The possibility of auto-intoxication is suggested by the constipation and a well-marked indican reaction in the urine. The case is very similar to Gowers' second case.

In the second, a boy, æt. 14 years, the initial symptoms consisted of a tingling of hands which spread up the arms; a tingling of feet spreading

up the legs; abdominal pain, and headache. These aural symptoms may last for some minutes, and are succeeded by a fall and unconsciousness, or rather modified consciousness. The boy lies quiet, with no spasms of any sort; his face is pale, with a grey colour round the mouth. If spoken to he is able to answer with difficulty. His mother has had three fits herself; her brother and her sister's daughter are confirmed epileptics.

In the third, a man, æt. 42 years, a sensation described as of a ball of air rising from the stomach into the throat is succeeded by a feeling of collapse and sometimes loss of consciousness (*petit mal*). Usually, however, the sensation is succeeded by a feeling of numbness of legs, which may become quite cold, and a coldness and numbness of fingers. The condition in the fingers is evidently closely allied to, if not identical with, Raynaud's disease, as they have at times become "as blue as a dark blue serge suit." This numbness and coldness of legs may last for two or three hours.

In the fourth, a man, æt. 39 years, has always been prone to ordinary fainting fits, and on one occasion he fell with absolute suddenness and without warning. In addition he has had several attacks in which he wakes up from sleep with a dizzy, swimming sensation, or with singing noises in the head. He vomits, and for a time varying up to a few hours is in a state of utter collapse and semi-consciousness. His hands and feet are always very blue and cold in cold weather.

Dr. H. G. Langwill* records two interesting cases.

The attacks in one, a woman, æt. 48 years, begin with a sinking feeling in the umbilical region and an overpowering sensation as if she were dying, consciousness, however, being always intensely alert, though the power of speaking, or even moving, is lost. The attacks come on chiefly on getting into bed. Seen in one attack she was extremely pale with a rapid pulse of markedly small volume, unable to speak, but acutely conscious of her surroundings. She was also subject to a severe "sinking feeling" constantly following upon evacuation of the bowels, so much so that she had to lie down immediately after stool.

In the second patient, a woman, æt. 38 years, the attacks also come on at bed-time with an intense feeling of "sinking," with a sensation of utter loss of all power and a feeling as if she were dying. Consciousness is always perfectly retained, face pale. For years she had always suffered on getting into bed at nights from sensations of pricking and numbness in hands and feet.

In the first case the blood-pressure was 110 and 120 on two occasions and in the second 90. On the supposition that the attacks were due to sudden dilatation of the vessels in the splanchnic region the effect of an abdominal binder with a large pad on going to bed was tried. In both cases this was extraordinarily successful.

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* "Note on the Treatment of a Type of so-called 'Fainting Attack,'" 'Edin. Med. Journ.,' August, 1908, p. 116.

Such cases are doubtless much commoner than is suspected, their somewhat indeterminate character and the absence of symptoms between the attacks making them difficult of recognition.

The onset is commonly sudden. The salient features are cardiac and vaso-motor with some modification of consciousness in the large majority of cases. There is obvious vaso-constriction of the cutaneous vessels in the majority of cases, as evidenced by pallor of face, coldness of extremities and tingling. Coldness of extremities was noted in eight of Gowers' eleven cases. It was present in a marked degree in two of my own. Pricking and numb feelings of hands and feet are probably also the result of vaso-constriction. They are common in the extremities in gross arterial disease.

The feeling of suffocation and the orthopnœa noticed in several of Gowers' cases are very interesting. Their nature is obscure, but it may well be that they are pulmonary in origin. The lungs contain a very capacious system of vessels, and Brodie* has shown that cardiac changes and variations in the systemic circulation can very materially alter the volume of blood contained in the pulmonary vessels. These cases exhibit obvious changes both in the cardiac and systemic systems. Vaso-dilatation in the splanchnic area is almost beyond dispute in many of the cases, although we cannot directly inspect the splanchnic vessels. The dis-

* "Lectures on the Pulmonary Circulation," 'Lancet,' March 22nd, 1902.

tribution of blood is disorganised over the whole body and engorgement (or anæmia) of the pulmonary vessels is very possible, and in cases in which it occurred would be a feasible explanation of the dyspnœa observed. Bronchial spasm may possibly participate in its causation.

Splanchnic dilatation is suggested directly by the disappearance of the blood from the cutaneous surface, factors of very common concurrence, and also by the copious diuresis following the attack in Gowers' second case. Rapid and rather persistent splanchnic vaso-dilatation is evidently a very important factor in these cases. This view is supported by Langwill's observation of the benefit attending the use of a firm abdominal binder, a procedure, moreover, which raised the blood-pressure 20–30 mm. of mercury in his first case.

The variations in the symptoms and in order of sequence depend in my opinion on the position of the vascular area primarily involved and on the nature of the vascular crisis. An initial splanchnic vaso-dilatation with lowered blood-pressure would clearly explain some cases. A severe initial vaso-constriction, for instance in the extremities, with rise of blood-pressure may possibly occur in some cases of so-called vaso-motor angina, though Dr. James MacKenzie found that the blood-pressure was not raised in some cases he had the opportunity of examining in an attack. Sir Douglas Powell in his article on this subject in Prof. Allbutt's 'System of Medicine' notes the same cardio-vascular in-

stability and the same physical and mental relationships. Dr. James MacKenzie discusses these abnormal circulatory disturbances under the very non-committal title of the "X Disease."* Pal has ably demonstrated the importance of vascular changes in relation to clinical symptoms in an exhaustive monograph — giving these changes the suggestive name of "Gefässkrisen"—vessel crises.

It is difficult to decide in each case whether the coldness of the skin is due to active vaso-constriction, or whether the skin vessels are merely narrowed down just enough to accommodate the diminished amount of blood available for them. On general grounds vaso-dilatation in a large vascular area which would cause lowering of blood-pressure is compensated for by active constriction in other regions. The tightening of the skin described in one case was possibly due to a contraction of the hair muscles.

Whether there is a very active vaso-constriction of the cutaneous vessels, it is clearly ineffective against the splanchnic dilatation, for it can scarcely be doubted but that the blood-pressure must usually be very low in these attacks. The pulse is usually extremely feeble. With a great accumulation of blood in the splanchnic region the pulse of necessity becomes small, and the common physiological accompaniment of a lowering of blood-pressure is an acceleration of the heart. But in

* Diseases of the Heart,' 1908, p. 56.

some of these cases there may be active cardiac inhibition as well.

Vaso-constriction in the splanchnic region doubtless occurs at times, but it is not yet an easily recognised factor in medicine. It is probably concerned in some of the attacks known as abdominal angina. So far as this condition can be demonstrable it was shown in a case observed by Capps and Lewis.* They were aspirating a pleural effusion in a man, æt. 30 years. Blood-pressure at the commencement was 120 mm. of mercury. Two litres of serous fluid were withdrawn, the blood-pressure falling to 105. The needle then came suddenly in contact with the visceral pleura and the patient complained of dull pain in the epigastrium, but of none in the chest. The pain grew rapidly worse and the blood-pressure rose steadily to 155 in the course of five minutes. Upon withdrawal of the needle the epigastric pain gradually subsided and the blood pressure was simultaneously lowered. Twelve minutes after the maximal anginal pain the blood-pressure had returned to 108 and the pain was gone. The authors conclude that excitation of the visceral pleura had in this case caused a reflex vaso-constriction in the abdominal arteries. I mention this most valuable observation because in the present ignorance of the type of cases we are discussing it

* "Observations upon Certain Blood-pressure Lowering Reflexes that arise from Irritation of the Inflamed Pleura," 'Amer. Journ. of Med. Sci.,' 1907, vol. cxxxiv, p. 890.

would be unwise to assume splanchnic dilatation to be invariable. The circulatory system offers abundant field for variation, and seeming contradictions may simply be due to varying phases of cardio-vascular behaviour and variations in the blood distribution.

In some of the cases consciousness has been modified—a dreamy mental state may be present, and a feeling of impending death is not uncommon. The extreme weakness of the pulse indicates a vascular depression that must of necessity affect the brain, and we know too little of the nature of mental processes to predict what alteration should attend a diminished blood flow. Momentary loss of consciousness occurs occasionally, as in some of Gowers' cases, and when it occurs he regards it as epileptic in nature, as *petit mal*. The unconsciousness may be an early or a late symptom in the attack, and in my opinion simply represents the fact that when it occurs the vascular depression has reached a point incompatible with consciousness, and that this is the missing link connecting it with epilepsy. Cerebral vaso-constriction may account for it in some cases, cardiac inhibition and low blood-pressure in others.

Further the prolonged symptoms in these cases are often of a type which, if of momentary duration, would be fairly characteristic epileptic auræ. At the same time, as has been pointed out, many of them are obviously vaso-motor or cardiac in origin, and that this is recognisable is due to the fact that

they are exceedingly deliberate in onset instead of sudden. If they were of slightly shorter duration and of greater intensity the epileptic relationship of these cases would be still clearer. Finally, if the cardio-vascular changes were absolutely sudden in onset, severe in degree, and transient in duration, they would be increasingly difficult of recognition and the epileptic nature of the attack unquestioned.

Gowers, of course, recognises that many of these cases present distinctly epileptic phenomena, and remarks that "velocity is an essential element of ordinary epilepsy, but this does not preclude the possibility of deliberation in attacks not far removed from epilepsy."

The Suddenness of some Faints.

Whilst the onset of an ordinary faint is gradual, in some cases it is rapid and may be absolutely sudden. A man very subject to ordinary faints on one occasion suffered from a sudden attack. He was sitting down and feeling perfectly well when he fell absolutely suddenly and bruised his face on the ground. Gowers also remarks that those who are prone to faint become after a time liable to do so more suddenly. In such cases there can be no question as to the nature of the attack. The vascular depression responsible for the ordinary faint must have occurred with greater rapidity. The suddenness suggests that a transient and sudden cardiac inhibition occurred rather than

that the attack was due to splanchnic vaso-dilatation. An isolated attack of unconsciousness sometimes with muscular spasm is not an unknown event in people showing no other signs of any tendency to faints or fits. Sudden cardiac inhibition supplies the most likely explanation of these attacks.

The Conversion of Fainting Fits into Epileptic Fits.

Gowers has recorded three cases in which repeated syncopal attacks have passed into epilepsy.* Thus:

"A girl when about 7 years old became liable to faint on any sudden start or alarm. The faints had all the character of cardiac syncope. There were pallor, coldness, and gradual loss of consciousness. After some years such faints occurred without exciting cause, and became more sudden in onset. When she was seventeen years old one of these attacks passed into a distinct epileptic fit with deviation of the head, general clonic spasm, and micturition during the attack. Others followed."

The second case was that of a woman, æt. 34 years, who "had been liable for twelve or more years to apparently true fainting attacks caused by excitement, over-fatigue, or a hot room. They began with palpitation of the heart and a sense of faintness, followed by gradual loss of consciousness, which did not become complete if she was able

* 'The Borderland of Epilepsy,' 1907, pp. 8 and 9.

promptly to lie down, when she always began to recover. At the age of twenty-five years these faints changed in character. She became unconscious more suddenly, and without any exciting cause; indeed, the onset was so abrupt that she only knew she had had an attack by finding herself on the floor. Recovery was then by mental confusion, not lessening faintness, and at first she could not tell where she was."

The third patient "was a woman who became prone to faint in early girlhood, especially in hot crowded places. In these she first became pale, felt faint, and gradually lost her sight, and then, if she tried to stay where she was she lost consciousness. Usually when sight had failed with help she was able to walk out of the place. During the effort dim sight returned, and the fresh air quickly restored her. These are the typical symptoms of cardiac syncope. Such faints continued until she was thirty years of age, when she became liable to sudden brief loss of consciousness, in which she often fell and sometimes hurt herself. After these she usually slept, and could not afterwards recall what had happened between the attack and the sleep. One occurred in a room with the door locked; the noise of her fall alarmed her friends, who knocked at the door. She got up and opened it, then she lay down and went to sleep, but afterwards remembered nothing of the incident. Such attacks were undoubtedly epileptic, and after they began she ceased to be liable to the faints.

She never had a convulsive seizure, but the attacks continued until she came under treatment at forty-two years of age, when they were arrested by bromide. She has since continued free. There was no heart disease and no family history of epilepsy, and no cause could be ascertained except the apparently disposing influence of the cardiac faints."

In all three cases the same phenomena were presented, attacks originally brought on by external influences and typically syncopal after a lapse of time appearing spontaneously and with a more sudden onset—in fact becoming undoubtedly epileptic.

The explanation of this change that naturally suggests itself is that the increased suddenness of the attacks is due to an increase in the rapidity with which the circulatory changes are brought about.

The symptoms of syncope are certainly due to cardio-vascular changes with alteration in the cerebral circulation, and an increase in the velocity of change would fully account for the suddenness of the unconsciousness. Gowers, however, postulates a change in the nerve elements of the brain as underlying the loss of consciousness in syncope, produced not directly by the failure of the circulation but rather by a sudden diminution in the intra-cranial pressure resulting from the circulatory failure.

He also states that "we have to conceive it"

(*i. e.* a change in the nerve elements) "as occurring spontaneously in epilepsy and as due to a sudden diminution in the intra-cranial pressure in syncope," and further that these cases in which repeated syncope seems to pass into minor epilepsy "suggest that the state of the nerve elements that underlies the loss of consciousness in syncope may, by repeated induction, acquire a tendency to spontaneous development, which constitutes minor epilepsy."

I submit that by frequent repetition the "resistance" of the nervous mechanism of the cardio-vascular apparatus is diminished, the reflex becomes easier and the failure of circulation occurs with greater rapidity, with the result that the loss of consciousness is proportionately more sudden. The distinction is one of the greatest importance, for the one view assumes a suddenly developing, mysterious state of the nervous system in which it becomes liable to sudden causeless failures of its activity, causeless in the sense that they are now independent of the circulatory failure admittedly producing the earliar attacks, whilst the other view affords an explanation of these attacks more in accordance with their clinical history.

So far we have considered the ordinary fainting fit. We have seen that definite subjective sensations or auræ may attend its onset, that it is often associated with vaso-motor instability, that it may be very sudden in onset instead of gradual, and finally that it may change in type and become

epileptic in character. In other groups of cases we have seen marked cardiac and vascular instability with the development of a series of symptoms depending directly on these cardiac and vaso-motor changes. Many of these symptoms are identical with epileptic auræ though more prolonged. We have seen that consciousness may be preserved though modified, that it may almost vanish, and finally that unconsciousness may develop. In all these cases the pathological variations in the circulation are such as to fully account for the unconsciousness and for the epileptic character of some of them.

The phenomena attending a sudden transient and demonstrable arrest of the heart should afford valuable evidence as regards the influence of sudden cerebral anæmia in the production of symptoms. These phenomena can be studied in cases of heart-block.

Cessation of the Cerebral Circulation.

I. *Sudden and Transient.*

(*a*) *Heart block.*—Alfred Webster* records a case accompanied by a series of sixty beautiful sphygmographic tracings which establish beyond question the fact that arrest of the heart preceded the epileptiform attack.

"From the sphygmographic tracings it was seen

* "Cardiac Arrhythmia in Relation to Cerebral Anæmia and Epileptiform Crises," 'Glasgow Hosp. Rep.,' 1901, vol. iii, p. 413.

that there were long intervals during which no pulse was appreciable at the wrist. These intervals sometimes lasted for ten or fifteen seconds. If the finger were kept on the pulse the following facts were observed and noted in order of their appearance: First the pulse became suspended, then, and almost at the same moment, the face became rapidly and extremely pale. If the period of absence of the radial pulse were only of short duration, say of four or five seconds, there was a general *crescendo* return of the pulse and a coincident flushing of the face. During these short pauses the patient appeared to be merely sleeping. Frequently, however, the period lasted much longer, ten, fifteen, and twenty seconds elapsing between the pulse beats. During this time, commencing with the disappearance of the pulse, the pallor of the face became more and more marked. Later on, however (perhaps after some fifteen seconds of absence of pulse), spasmodic twitchings of the face were observed; then as the period lengthened the spasmodic movements extended to the muscles of the neck, frequently carrying the head to one or other side, and ultimately the arms and legs took part in the convulsive movement. Flushing of the face and the return to consciousness were always almost simultaneous with the appearance of the pulse at the radial artery, the pulse being felt slightly before the flushing of the face was observed. Auscultation over the præcordium during these pauses discovered what

appeared to be abortive beats of the heart, but these beats were not appreciable to the finger at the radial pulse, or indeed in any of the superficial arteries."

Dr. George Murray,* in his Bradshaw Lecture on "Exophthalmic Goitre," describes the case of a young woman, æt. 22 years, whom he was treating with the preparation of dried milk of thyroid-ectomised goats, known as "rodagen." Whether the result of the rodagen or not, she developed sudden cardiac failure with bradycardia, and one day "between 7.20 and 11 a.m. she had numerous attacks, in each of which the heart, which was, as already described, beating slowly, would stop altogether for several seconds; a convulsion then took place, which lasted two or three seconds. The patient was conscious at the onset of the convulsion, but lost consciousness for a second or two at the end of it. One or two of these attacks occurred while I was auscultating the heart, and the long period of asystole was remarkable; the slow pulse was irregular at the time. After 11 a.m. she had no return of the attacks."

A very good example is recorded by Hay and Moore,† in which the convulsive movements "varied from slight twitching movements and rigidity to a *severe general convulsion*." In their case the periods of ventricular asystole were at

* 'Brit. Med. Journ.,' 1905, vol. ii, p. 1379.

† "Stokes-Adams' Disease and Cardiac Arrhythmia," 'Lancet,' 1906, vol. ii, p. 1271.

times as long as seventy-five seconds. The convulsive movements always came on towards the end of the seizure.

Another most instructive case was recorded by Finny.*

The patient was a woman, æt. 42 years, who suffered from bradycardia and arrhythmia of the heart from April, 1904, to March, 1906. Without entering into any details as to the cardiac condition, it may be stated that the pulse-rate was, as a rule, between 21 and 28 per minute. At varying intervals, however, the rate changed, and a state of pulselessness lasting from five to fifteen seconds supervened. During these latter periods certain fits, or, as she described them, "weak turns," developed. Frequent observations determined the fact that the fits were not simply due to the infrequency of the pulse, for they did not occur while the pulse-rate was as slow as 18 or 20 per minute, but that they were sure to occur when pauses of eight to ten or fifteen seconds were observed, and that they occurred towards the end of the period of cardiac asystole. Dr. Finny gives the following description of the fits:

"A 'weak turn' was ushered in and preceded by a delay in the heart's beat and radial pulse. Thus when a pause lasted seven to ten seconds the patient's face became pale, the eyes had a very pained and frightened look, and some little

* "Bradycardia with Arrhythmia and Epileptiform Seizures," 'Brit. Med. Journ.,' 1906, vol. i, p. 1112.

restlessness of the head and hands ensued, and it ended by a slight flushing of the cheeks, some tears in the eyes, and the patient would give a slight sigh, or little hem or cough, and the weakness would be over. The 'slight fit' came on with a soreness or sharp feeling in the stomach and left side of the thorax, which would then extend up the right side of the chest into the head and eyes. The pallor of the face would be more marked, the eyes would turn up to the right side, and the hands would fidget and the fingers catch at the sheets. The patient always came out of this fit in a more frightened and slightly dazed manner, and the eyes had a strained and somewhat blind look for some minutes. The 'severe fit' was more distinctly epileptic with sudden onset, the patient falling back if sitting up in bed, great pallor, convulsive movements of hands and arms, and also slightly so of feet, unconsciousness for five or ten seconds, and then great flushing of the face, and the patient came out of it very confused, and she was dull and nervous the whole day following. She never bit her tongue or passed urine in them."

Many other cases could be quoted, but the above are enough to justify the statement that cessation of the heart for a limited number of seconds is associated with transient loss of consciousness which may be absolutely indistinguishable from *petit mal* (indeed, Finny regarded and treated his patient for such on first seeing the case), and that with more prolonged cardiac arrest

definite convulsive seizures are brought about, which may be practically indistinguishable from those of major epilepsy.

In such cases of heart-block, moreover, the cardiac arrest is the result of heart disease. That the unconsciousness and convulsions in these cases are directly dependent upon a primary failure of the cardiac contraction, and therefore of the cerebral circulation, is obvious.

If evidence is forthcoming that in idiopathic epilepsy a comparable failure of the cerebral circulation occurs, the evidence will be strong that, as in the cases above recorded, the relation between the circulatory failure and the fits will be one of cause and effect. Such a sudden failure in the cerebral circulation might be due to a sudden cardiac inhibition or to a sudden vaso-motor spasm in the cerebral arteries. We will consider both possibilities.

Evidence of Cardiac Arrest in Idiopathic Epilepsy.

Moxon* records three cases in which an epileptiform attack followed an arrest of the heart's action. In only one case was the patient an epileptic, but they are of such value that I will quote them all. In the first he was examining a patient with cardiac dropsy:

"I was feeling his pulse carefully; the beats

* "On the Influence of the Circulation on the Nervous System," 'Lancet,' 1881, vol. i, p. 648.

were regular and of moderate strength. . . I missed one, then another beat, and then found the pulse to have stopped so entirely that it made me look up suddenly at the man to see what was the matter. His face had become very pale, his head was turned towards his left shoulder, and the lip and cheek were twitching; the spasms then affected his arms, and he passed into a severe epileptic convulsion. At the time when I first noticed the pulse to disappear the man's arm was quite still. I tried to feel the pulse during the convulsion, but there was so much muscular movement that I could not distinguish it."

On another occasion Moxon was examining the pulse of a man who had been admitted to hospital for uræmic vomiting and convulsions:

"I took his wrist and felt his pulse; it was forcible and regular. I was feeling it when it disappeared from under my finger, many beats being missed. I looked at him; he had become very pale in the face, twitching set in, and he at once went into a very severe epileptic convulsion."

Moxon's house-physician, Mr. Lane, corroborated the same fact twice on the same patient.

Moxon noted a third example in an epileptic:

"I was examining the heart of a young gentleman who was asking my advice on account of attacks of epilepsy. He was standing and I had my stethoscope over his heart and was attending to the quality of the sounds. These sounds stopped suddenly and so completely that in great surprise

I moved to look at him, and saw him with exceedingly pale face, evidently quite unconscious, his balance just lost and he falling forwards. He forthwith went into severe epileptiform convulsions."

At the conclusion of his lecture Dr. Southey informed Moxon that, in the only instance in which he had his finger on the pulse at the beginning of an epileptic convulsion, he observed the pulse to disappear during the onset of the attack. Moxon further remarks that—"I have found the pulse present again when the clonic spasms have just commenced." He attributed the cessation of the heart to the action of the pneumogastric nerve, but recognised the fact that the cause of this pneumogastric impulse was yet to seek.

Hilton Fagge* records a similar case. He was listening to the heart of an epileptic when it ceased to beat and the man fell back. Presently it recommenced to beat, and then there was a little twitching of his hands.

The writer† has recorded a similar case coming under his own observation, and another communicated to him:

"The patient, C. T.—,was a man, æt. 21 years. He had suffered from epileptic fits all his life. A

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* Fagge and Pye-Smith, 'Text-book of Medicine,' second edition, 1888, p. 793.

† Alfred Russell, "Cessation of the Pulse during the Onset of Epileptic Fits, with Remarks on the Mechanism of Fits," 'Lancet,' 1906, vol. ii, p. 152.

maternal aunt had also been subject to fits all her life. The patient's fits commenced with an aura, which was referred to by him as an indescribable sensation in his navel. The majority of his fits occurred in bed at night; sometimes in his waking moments. Any emotional excitement was very apt to precipitate a fit. On April 21st he developed a fit in the out-patient room. He uttered a cry and was seen to be rubbing his hands together. His pulse was immediately examined for, but was not palpable. He was just commencing the stage of tonic spasm when the wrist was seized. Dr. E. W. Hedley, who examined the other wrist, also corroborates the absence of the pulse during the tonic phase. It was not easy to determine exactly when the pulse returned, but we feel certain that the pulse did not return until the clonic phase. At first it was feeble, but as the fit subsided it became fuller and stronger."

Dr. W. T. Harris, of Chiswick, has kindly told me of another case which occurred in his practice.

A man came to have a tooth extracted. While applying the forceps the patient's head suddenly fell back and his face turned exceedingly pale. On feeling for his pulse Dr. Harris found it to be absent. Thinking that it was a severe syncopal attack he attempted to give the patient some sal volatile, but clonic convulsions intervened. These were slight and very transient, consciousness being regained almost immediately. Within a few minutes, however, the patient again turned very

pale and became unconscious with toxic spasm. Dr. Harris again noted complete absence of the radial pulse, but at the commencement of the clonic stage a feeble pulse appeared at the wrist, which gradually improved as the fit subsided. On questioning the patient he acknowledged having had two previous epileptic fits.

The peculiar significance of this case lies in the fact that the complete absence of the pulse and the patient's extreme pallor led Dr. Harris to believe that it was a fatal attack of syncope.

It is not contended that complete cardiac arrest occurs in every epileptic convulsion, for it is stated that the pulse may persist throughout a fit, but an extreme feebleness, short of absolute cessation, might be sufficient to initiate a fit. The following case for example, which occurred under the author's own observation, might well be described as a fainting fit but for collateral evidence.

The patient, T. A—, was a youth, æt. 20 years. He came to hospital having had a "fit" the previous day. He had had only one fit previously, twelve months ago. His facies, however, was typically epileptic. He attended hospital for three weeks, and during that time had one more attack. On his last attendance he complained of pain over a subaceous cyst situated over his right mastoid process. His pulse was 74 per minute, but was small and rather feeble. He flinched on examination of the sebaceous cyst, turned very pale, and rolled back in the chair unconscious. His pulse

was found to be extremely feeble. There were no spasms whatever and the unconsciousness lasted for about a minute, when he gradually regained his senses. This attack could only be called a faint. In two or three minutes, however, he again turned pale and fell back, but with this difference, that there were several clonic spasms of his face and one spasm in his arms. His pulse was under examination when he rolled back, and it became so feeble during the period of unconsciousness as only to be detected with considerable difficulty. He was stupid for a few minutes and then recovered. After the attack was over his pulse was still very feeble, but on examination with the sphygmomanometer the blood-pressure was found to be 120 mm. of mercury.

Nobody seeing the boy and the second attack could doubt its epileptic nature, and at the same time the alteration in the pulse in both attacks left no room for doubt but that it was the precipitating factor both of the "faint" and of the "fit."

The Causation of Cardiac Inhibition in Epilepsy.

Moxon attributed the cardiac arrest in his cases to a vagus inhibition of the heart.

Dr. F. H. Clarke,* in a paper on "Epileptoid

* F. H. Clarke, "Epileptoid Attacks in Tachycardia and Bradycardia," 'Brit. Med. Journ.,' 1907, vol. ii, p. 308. Quotes Langendorff: "Epileptische Krämpfe bei peripherer Vagus Reisung," 'Centralb. f. med. Wiss.,' 1878, vol. xvi, p. 65.

Attacks in Tachycardia and Bradycardia," quotes Langendorff's observations on the results of stimulation of the peripheral end of the vagus in rabbits narcotised with chloral: "Electrical stimulation of the peripheral end of the vagus causes a prolonged stoppage of the heart, with a very remarkable phenomenon, never hitherto observed, so far as we know,—a complete epileptic convulsion occurs ten or fifteen seconds after the diastolic pause. . . . Precisely similar convulsions are produced by compression of the thoracic aorta at a point nearer the heart than where the great vessels are given off to the head."

Francis Hare* also attributes the epileptic fit to a cerebral anæmia, the result of vagus inhibition of the heart, and assumes further that the inhibition is a reflex act secondary to a widespread vaso-constriction.

There is no doubt that *in epilepsy the vaso-motor system is unstable.* I have been repeatedly struck by the pulse irregularities in epileptic patients. In some the pulse-rate is, as a rule, very considerably increased, and yet on other less frequent occasions it is abnormally slow. Not only that, but the pulse frequently shows wide variations in the course of a few minutes. In two patients I have seen time after time the pulse so feeble and small that they might, on the evidence of the pulse alone, have

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* Hare, 'The Food Factor in Disease,' 1905, vol. i, pp. 331, 332.

been in a state of severe collapse. The volume and pressure also vary very considerably. These variations are just as well marked in old cases inured to hospital as in new ones, in whom the pulse might be affected directly as the result of their visit to a hospital.

Spratling* notes that:

"In 284 cases in which the pulse-beat was noted it was found to run uniformly above the normal in 189—64 per cent. In 20 cases it was below 70; in 74 cases from 70 to 80; in 161 cases from 80 to 100; while in the remaining 29 cases it was 100 or over. It was counted in every instance during the interparoxysmal period, the patient being entirely free from any immediate epileptic influence."

In an examination of thirty-three cases, to determine the blood-pressure as near to the convulsive period as possible and as remote from the same period as possible, Spratling found an apparent decrease in the blood-pressure just before the convulsive period in eleven cases, and an increase in twenty-one at the same period, the latter being somewhat more marked in degree than the former. The rapid rise in blood-pressure postulated by Hare as preceding the vagus inhibition might be very transient, and, unless the blood-pressure were under observation at the moment preceding the onset of the fit, would be most difficult of demonstration and even of observation. The sensatior

* Spratling, 'Epilepsy,' 1904, p. 271.

of chilliness which sometimes precedes a fit is presumably to be attributed to cutaneous vaso-constriction. If, however, constriction should occur in other regions—the splanchnic area, for instance, or in a large muscular area—the result would be the same, viz. either a compensating vaso-dilatation elsewhere, or of necessity a rise in the general blood-pressure. If, instead of the heart responding to this rise in blood-pressure by the customary increased force of beat, its vagus mechanism were too sensitive, or its protecting depressor nerve mechanism at fault, the result might be cardiac inhibition with resulting cessation of the heart, or a marked enfeeblement short of actual cessation, followed by unconsciousness, and if of more than the most transient duration would result in the production of convulsions, *i. e.* an epileptic fit.

It is unfortunate that so few observations of these vascular changes in epilepsy are on record. Unless the heart or pulse happens to be under examination at the moment of onset of a fit the opportunity does not occur, the failure of the circulation is very transient, and the muscular spasms render any examination of the heart and pulse a matter of great difficulty.

It is maintained in these lectures that the fundamental factor underlying both the ordinary faint and the epileptic fit is cerebral anæmia. It follows further that the difference between the two is one of degree rather than of kind. We have had some clinical evidence of this in the

suddenness of some faints and in the conversion of faints into fits. The difference I hold to be due to the difference in the rate of development of the cerebral anæmia. In the ordinary faint the cerebral circulation slowly diminishes *pari passu* with the falling blood-pressure. In the fit there is a sudden cessation of the circulation. Similarly the circulation slowly improves in the faint; in the fit it probably returns with greater rapidity.

The fainting proclivity is commonly associated with other evidences of cardiac and vaso-motor instability and an exciting cause is usually present. In epilepsy the ordinary evidences of vaso-motor instability are not so obvious and exciting causes are commonly absent, or rather unrecognised. It must suffice for the present to bring forward the above evidence of cardiac inhibition, however scanty, and to examine to what extent it will explain the various manifestations of epilepsy.

The Correlation between the Circulatory Changes Postulated as the Precipitating Factor in the Epileptic Fit and the Various Symptoms of, and the Recovery from, the Attack.

For any theory of the mechanism of the epileptic fit to rest on a sound basis it is necessary that it should offer a reasonable explanation of, or at least not to be inconsistent with, the various manifestations observed in the attacks. It is submitted that the circulatory failure above postulated does

offer a more reasonable explanation than any hypothesis yet brought forward.

(1) *The aura.* — Francis Hare maintains that the explanation of the aura is to be sought in the peripheral vaso-constriction which he postulates as preceding the cardiac inhibition.

"The vascular changes, occurring as they do, synchronously with the rise of blood-pressure, offer a reasonable explanation of the epileptic as they do of the migrainous, asthmatic, and other auræ. Some of the vascular changes may be peripheral and constrictive. Fagge* says: 'The patient perhaps experiences a sensation of coldness or weight in the limb, and the part is found on examination to be pale and cold to the touch, and to have its sensibility distinctly blunted.' Others of the vascular changes may be peripheral and dilative. Trousseau† says: 'A local determination of blood may occur in the finger for instance, causing it to swell, reddening the skin, and rendering it successively within a very short time red, and of a more or less deep violet colour. . . . The swelling is real, not apparent, for rings previously easy suddenly become too tight for the fingers.' Or, again, vascular dilatation and vascular constriction may alternate. Trousseau says‡: 'The skin may become excessively pale after having been injected for some time.' But many

* Fagge, 'Text-Book of Medicine,' 1891, vol. i, p. 751.

† 'Clin. Medicine,' New Syd. Soc., vol. i, p. 61.

‡ *Ibid.*

auræ are unassociated with appreciable objective changes in the part whence they seem to arise. Then it is not unnatural to believe that invisible vascular changes similar in character to the visible peripheral vascular changes just described are taking place in the cerebral centres, and are the immediately responsible factors."*

That a partial cerebral anæmia is capable of giving rise to the phenomena of an epileptic aura has been demonstrated experimentally by Leonard Hill,† who says: "I myself have twice produced clonic spasms in myself by compression of one carotid. The first effect on applying the compression was a *sensation in the eye on the same side, then there followed a sensory march of formication down the opposite side of the body. This began in the fingers, spread up the arm, then down the leg.* Finally clonic spasms of the hand occurred, accompanied by an intense feeling of vertigo and alarm."

The association of epilepsy with migraine is well known, and in a unique case recorded by Gowers of a girl who was subject to both migraine and epilepsy, the visual aura preceding the migraine was on one occasion followed by an epileptic fit.

It has been pointed out that some of the prolonged symptoms in the more abnormal faints were obviously vaso-motor or cardiac in origin, and

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* Francis Hare, 'The Food Factor in Disease,' 1905, vol. i, pp. 335, 336.

† 'The Physiology of the Cerebral Circulation,' p. 142.

yet were they of momentary duration they would be typical epileptic auræ. Or, as Gowers puts it, in discussing one case with attacks of cardiac and respiratory distress: "Symptoms usually momentary, as the aura of epilepsy, become protracted, extended, as it were into a vagal attack."

(2) *Unconsciousness.*—In the absence of an aura (and it is noteworthy that it frequently is absent), the first feature in an epileptic fit is sudden loss of consciousness. So sudden may it be that the patient falls with the utmost violence. Current views on the pathology of epilepsy afford no satisfactory explanation of this. Yet so dramatic a feature should be susceptible of some simple explanation. The loss of consciousness is not caused by the convulsions. It precedes them in point of time, and in tetanus and strychnine poisoning the spasms may be every whit as severe as those of idiopathic epilepsy, but are not attended with unconsciousness. Now one of the most obvious causes, if not almost the only one, of sudden unconsciousness (excluding severe cranial injuries), is a sudden interference with the flow of blood to the brain. And even in the case of cranial injuries Cannon has concluded that the primary unconsciousness is the result of a cerebral anæmia from reflex cardio-vascular changes.*

The phenomena of the epileptic fit are commonly explained as being the result of an intense

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* 'Amer. Journ. of Phys.,' 1902, vol. vi, p. 91.

discharge from the cortical grey matter. On the motor side this discharge leads to severe muscular spasms, to excessive if disordered function.

As regards consciousness this is absolutely and suddenly lost. I cannot understand how this can be caused by a discharge. It seems to me that the very opposite factor, viz. cessation of activity, must be involved. Consciousness is, I think, too commonly regarded as too mysterious to be governed by ordinary physiological processes, but the brain is certainly very tenacious of this attribute, and a symptom so extraordinarily dramatic and serious as sudden unconsciousness demands an explanation. Save for conditions associated with the vascular system such as cerebral embolism, stoppage of the heart, sudden faints, etc., sudden unconsciousness is almost unknown.

But with a *sudden cessation (or extreme enfeeblement) of the whole cerebral circulation* unconsciousness *must* occur. The phenomena of heart-block show that, in proportion as the period of cardiac asystole increases, we have varying degrees of cerebral failure, transient unconsciousness indistinguishable from that of *petit mal*, attacks with very transient spasm, and finally, definite epileptic fits. Inasmuch as it has been shown that in some cases of idiopathic epilepsy cardiac inhibition does occur, and precedes the onset of the fit, it is difficult to avoid the conclusion that the unconsciousness and fit are the direct results of the cardiac inhibition.

It is noteworthy, also, that sudden occlusion of one large cerebral artery by an embolus produces sudden unconsciousness. A complete cessation of the entire cerebral circulation following upon cardiac inhibition would be obviously a still more potent cause.

In the next lecture the discussion of correlation between the circulatory changes and the phenomena of an epileptic fit will be continued, and the symptoms produced by a more prolonged arrest of the cerebral circulation will be described.

LECTURE II.

Mr. President and Gentlemen,—In the last lecture I dealt first with the ordinary fainting fit, showing how it can merge by insensible degrees into an attack indistinguishable from an epileptic fit. I also dealt with certain prolonged attacks, and I endeavoured to show that the cardiac and vaso-motor irregularities, which were the predominant features in the attacks, might fairly be considered as responsible for the varying clinical phenomena and for the epileptic phenomena which were present in some. The influence of arrest of the heart with resultant failure of the cerebral circulation in producing attacks, varying in degree from transient unconsciousness to a severe convulsive fit, as evidenced in cases of heart-block, was adduced. Evidence of cardiac arrest in some cases of epilepsy itself was adduced. Lastly the feasibility of the hypothesis was being tested by an examination as to whether it was capable of explaining, or at least of being consistent with, the various stages of an epileptic fit. I discussed the aura and the unconsciousness. Following these symptoms comes the stage of convulsions. The failure of the heart cuts off the supply of blood not only from the brain but also from the spinal cord and the entire musculature of the body, and the patient falls suddenly.

Convulsions.

The classical experiments of Kussmaul and Tenner prove the intimate relationship existing between a sudden cerebral anæmia and the production of convulsions. Their experiments, moreover, were not masked by the administration of anæsthetics. It is also well known that severe hæmorrhage in man can give rise to a typical convulsive fit. This is not often seen nowadays, but in the old blood-letting times it was common enough, and Marshall Hall* remarks that "convulsion is, after syncope, the most familiar of the immediate effects of loss of blood."

(A) *Tonic spasm.*—It is well known that sudden death may occur during exploratory puncture of the chest. In a paper published by the author† on this subject three cases of death occurring during or after this procedure were recorded. In the first the insertion of the needle was immediately followed by sudden death from cardiac failure, and the point of interest in this connection is that it was accompanied by tonic extensor spasm of the arms and convergent squint. The condition of the legs was not observed, but it is very probable that they shared in the spasm. Similarly, as will be shown later, tonic spasm occurred in a case recorded by Cayley in which cardiac inhibition occurred during

* 'Observations on Blood-letting,' 1836.

† 'St. Thomas's Hospital Reports,' 1899, vol xxviii, p. 465.

pleural lavage. It also frequently occurs on experimental ligation of the cerebral arteries in animals. This spasm may depend on the removal of the inhibition influence of the brain, and is possibly allied to the decerebrate rigidity described by Sherrington in animals with transection of fore-brain. It might at first sight be supposed that such spasm should be seen at every death-bed, but in the large majority of cases death is a gradual process, the circulation failing by degrees, the nutrition and irritability of the brain slowly diminishing with the failing circulation, so that any sudden manifestation of spasm would hardly be expected to occur.

In an epileptic fit tonic spasm occurs with great suddenness, and this manifestation is therefore in accordance with what is seen in sudden circulatory failure.

(B) *Clonic spasms.*—In the case of sudden death after exploratory puncture of lung, just mentioned, only tonic spasm was observed. The change from tonic to clonic spasms in an ordinary epileptic fit is of great interest. Long Fox,* who attributed the loss of consciousness and the tonic spasm to cerebral vaso-constriction, ascribed the clonic convulsion to a "gradual yielding of the vaso-motor constriction, allowing at first more blood to enter the arteries than during the period of tonic spasm,

* 'The Influence of the Sympathetic on Disease,' 1885, p. 252.

but yet far less than is necessary for controlled movement or for rest." They will be referred to again in the next lecture. In this connection a case recorded by Walter Broadbent* is of great importance.

The patient was a lady, æt. 44 years, who had suffered from rheumatic fever in childhood, and showed symptoms of cardiac disease. For seven years she had been subject to epileptic fits. One evening, when talking to her daughter, she suddenly became unable to speak plainly and became rigid. The daughter stated that, instead of the usual fit, there was irregular jerking confined to the right arm and leg; the mouth was drawn over to the right, the head turned to the left. The left arm and leg remained absolutely passive. She passed urine in the fit. She was unconscious for five days after the fit. She then showed complete hemiplegia, hemianæsthesia and hemianalgesia. Movements and sensations were normal on the right side. Death occurred on the ninth day. Post mortem: in the right middle cerebral artery, just beyond the point of origin, a small embolus was found with a distal thrombus for half an inch. The cortex along the course of the vessel was softened; on section the right corpus striatum and all the surrounding parts, including a portion of the frontal lobe, were in a state of extreme softening.

* "Cerebral Embolus during an Epileptic Fit," 'Brain,' 1903, vol. xxvi, p. 447.

The importance of this case lies in the fact that the patient was the subject of epilepsy. It is presumable that the embolus gave rise to a fit in a subject prone to epilepsy, but the fit was represented by right-sided spasms only. The left side remained absolutely passive, and the embolus in the right middle cerebral artery would prevent the return of blood to the right half of the brain after the cardiac inhibition was passing away.

On the other hand, cerebral embolism is sometimes attended by tonic and clonic spasms of the contra-lateral side, and the absence of such in this case might be urged as evidence against the view that the clonic spasms are due to the return of the circulation. But convulsions are not invariable in embolism, and the obstruction to the circulation need not be complete; an embolus may be arrested at a given point without completely occluding the lumen of the artery. Both the degree of severity of the initial symptoms and the subsequent course of the case will depend on this. Loss of consciousness does not always occur in embolism.

In thrombosis unconsciousness and convulsions are much rarer. Owing to the gradual diminution of the lumen of the diseased vessel some degree of collateral circulation may have developed, and the related area of brain has probably adjusted itself to a diminished circulation, and lastly the terminal thrombosis obliterating the vessel may take a very definite time. For these reasons the shock is much less sudden and the nutrition fails rapidly rather

than suddenly, and spasm is much less likely to occur. We are, of course, referring solely to the initial spasm of cerebral vascular obstruction, which alone can be compared to the spasm of the epileptic fit. The subject of clonic spasms will be referred to again in the next lecture.

The Physiological Mechanism underlying Recovery from an Epileptic Fit.

Whatever be the immediate factor precipitating an epileptic fit, it is one which is very transient in its action and speedily recovered from. It is one, moreover, which is obviously capable of being brought into action repeatedly. In epilepsy of long duration the patient exhibits a very marked mental degradation, but the effect produced by each fit is imperceptible. Quite apart from the effect produced on the brain by the repeated attacks of cerebral anæmia here postulated as the essential factor of the fit, the intense venous engorgement resulting from the convulsive movements and the asphyxial character of the blood would presumably inflict considerable damage on the brain substance, damage, moreover, repeated over and over again. It would not appear unreasonable to assume that the slight morbid changes described in the brains of epileptics are merely the cumulative results of these lesions. Nothing is more striking than the completeness of recovery from an epileptic fit. Whatever the cause, it seems to pass away absolutely. On the supposition that

the fit is due to a sudden transient cerebral anæmia, produced by sudden and transient failure of the cardiac contraction, recovery follows on return of the circulation.

It might be urged that if the fits are due to such cardiac failure it should occasionally happen that the heart should stop permanently, and that death in a fit should be, at any rate, not unknown. If the cardiac arrest is due to vagus inhibition and if this inhibition is sufficiently intense, death might doubtless result, as in the case of sudden death recorded above on exploratory puncture of the lung. But though experimental stimulation of the vagus nerve with a very powerful stimulus does rarely produce permanent arrest of the heart, it is a fundamental physiological fact that there is a practically irresistible tendency for the heart to recommence beating, even during the stimulation—the so-called vagus escape of the heart. We must assume that during arrest of the heart the production of the stimulus material responsible for the initiation of the cardiac contraction, a function centred near the mouth of the superior vena cava, and also the excitability of the cardiac muscle, viz. its power of reaction to the stimulus material, progressively increase until they break through the restraining vagus influence and the cardiac rhythm is restored.

Or it might be that there is a failure of stimulus production with resultant cessation of cardiac activity until, with the accumulation of stimulus

material, the heart resumes its beat. Lest this sounds too speculative, I will anticipate what will be mentioned in the next lecture in dealing with status epilepticus, viz. that Mott, in his description of the hearts of people dying of status epilepticus, has described most marked alterations. The heart shows extreme fatty degeneration ; the fibres are separated from one another by a serous exudation ; they have a lustreless appearance, with indistinctness of striation and accumulation of minute particles of fat in the substance of the fibres. It is greatly to be desired that careful examination of the hearts of people dying of epilepsy should be made by those whose work gives them the opportunity.

This tendency of the heart to recover after arrest is submitted as a feasible explanation of the recovery from major fits.

Post-Epileptic Phenomena.

Though recovery may be very rapid after a mild fit, there is commonly observed after the cessation of the convulsive movements a period during which the patient is comatose, a period frequently followed by natural sleep varying in duration. On the hypothesis of a sudden failure of the cerebral circulation there has been a profound though temporary disturbance of the nutrition of the whole nervous system. As the result there has been an intense motor disturbance. The sensory side of the brain has doubtless been the seat

of an equally severe disturbance, the earliest sign of which is sudden unconsciousness. The initial anæmia of the brain followed by the intense venous engorgement attending the convulsions is enough to account for exhaustion of the sensory elements with resulting coma and sleep. These factors might equally be responsible for the mental disturbance following major attacks.

Those occurring after minor attacks, however, belong to a different category. Mental disturbance is much more common after minor than after major attacks. After major attacks there is commonly a period of coma followed by natural sleep which may restore the equilibrium of the brain. After a minor attack, however, the patient is immediately in full possession of his physical capacity, and any mental disturbance is therefore allowed full play. A very transient circulatory disturbance might well upset those delicate processes which constitute the normal adjustment of the individual to his environment. The exact pathology of such conditions is in the present state of our knowledge impossible of determination whatever view be taken of the pathology of epilepsy.

On Cerebral Intra-vascular Clotting as the Cause of the Epileptic Fit.

According to Dr. John Turner,* "Epilepsy is a disease occurring in persons with a defectively

* "The Pathology of Epilepsy," 'Brit. Med. Journ.,' 1906, vol. I, p. 496.

developed nervous system, associated with a morbid condition of the blood, whereby it shows a special tendency to intra-vascular clotting, and that the immediate cause of the fits is sudden stasis of the blood-stream resulting from the blocking of cerebral vessels by these intra-vascular clots." The objections to this view which I raised in a paper on the pathology of epilepsy, read before the Royal Society of Medicine in December, 1907, were : first, that these coagula might be the result of the fit; secondly, that it was difficult to explain the completeness of recovery and absence of paralysis after a fit, if such widespread thrombosis had occurred; and thirdly, that if the clotting were localised it was difficult to realise how it could bring about the extraordinary phenomena of a fit. In a more recent communication* Turner thinks that I have under-estimated the structural defect of the nervous system in epileptics, and that localised thromboses might be efficient in the presence of an easily excitable cortex, and that the absence of gross after-effects are to be explained by the fact that the thromboses occur in minute vessels for which collateral circulation might be readily available. The exact interpretation of the changes observed by Turner is not clear, but in that he attributes the fit to

* "Some Further Observations on the Supposed Thrombotic Origin of Epileptic Fits," 'Journ. of Ment. Sci.,' 1908, vol. liv, p. 638.

stasis of blood in the cortex we seem to be on common ground, viz. a sudden cerebral anæmia.

Some observations of L. S. Dudgeon * are of interest in this connection : " In the blood obtained from a case of long-standing epilepsy a striking instance of auto-agglutination was observed. The patient's serum, when added to his own red cells, caused a high degree of agglutination. The same effect was observed when the serum was added to normal red cells. In this specimen of blood we have one of the few examples and yet one of the most striking instances of auto-agglutination. In another case of long-standing epilepsy the immune serum failed to react in presence of the immune red cells or normal red cells, but when normal serum was mixed with the immune red cells they collected into large and tight lumps."

I have mentioned this interesting observation in this connection ; but it would be, in the present state of our knowledge, a most hazardous speculation to infer from observations on the behaviour of the blood outside the body that similar changes occur within the vessels of the brain.

On Vaso-motor Spasm in the Brain as a Cause of Epilepsy.

This theory of the method of production of cerebral anæmia as the cause of epilepsy has had

* " On the Presence of Hæm-agglutinins, Hæm-opsonins and Hæmolysins in the Blood obtained from Infectious and Non-infectious Diseases in Man," ' Roy. Soc. Trans.,' 1908.

many adherents. Hallager's monograph upholding this view gives a full historical retrospect.* If, as this paper is written to maintain, epilepsy is due to a sudden failure of the cerebral circulation, then vaso-motor spasm of the cerebral arteries, if intense enough, could certainly act as an adequate excitant of a fit. Direct demonstration of this as the excitant would obviously be very difficult, but if it can be proved that such vaso-motor activity does occur, the possibility of its being concerned in the genesis of some fits would be established. Until recently it was held that there was no evidence of vaso-motor activity in the cerebral vessels, but the demonstration of a copious network of nerve-fibres to the cerebral blood-vessels demands a revision of the position.

Harvey Cushing† notes that, "contrary to the positive statements of many, substances like epinephrin will blanch the pial vessels over the area of its application, as will occasionally a jet of cold water against the brain or the faradic current used for cortical stimulation."

Brodie and Ferrier‡ also found that on injecting adrenalin into the basilar artery of the carefully removed brain, and measurement of the outflow

* Hallager, 'De la Nature de l'Epilepsie,' 1897.

† Some Experimental and Clinical Observations Concerning States of Increased Intra-cranial Tension," 'Amer. Journ. Med. Sci.,' 1902, vol. cxxiv, p. 400.

‡ Ferrier, 'Harveian Oration,' 1902, "The Heart and Nervous System."

from the torn sinuses, with a moderate amount of adrenalin, distinct diminution of the outflow occurred, and with a larger quantity, complete stoppage.

The phenomena of Raynaud's disease are also worthy of study in this connection. The pathology of this affection is far from clear. In some cases there appears to be no doubt but that the symptoms are due to arterial disease; but it is generally admitted that vaso-constriction in the affected parts is the dominant factor. It is occasionally associated with erythromelalgia. Raynaud* observed that œdema may precede the attack of local syncope.

Certain ocular and cerebral complications occasionally occur in the course of the attacks of Raynaud's disease which are readily explicable on the supposition of an active constriction of the cerebral arteries.

Thus in Raynaud's new researches † a man, æt. 59 years, with attacks of local asphyxia, also suffered from paroxysmal attacks of impairment of vision. Ophthalmoscopically the arteries were found to be narrowed with here and there partial diminutions, which were actually seen to occur, persist for a certain time, and then disappear under the observer's eyes.

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* Raynaud, "On Local Asphyxia," New Sydenham Society translation, 1888, p. 172.

† Raynaud, *loc. cit.*, p. 155.

In another case of Raynaud's* a man, æt. 22 years, was subject to attacks of local asphyxia which occurred when the patient went into the open air. The patient also experienced *at the moment of the commencement of the cyanosis a notable obscuration of sight*, which disappeared at the time when the face and hands returned to their normal colour. Ophthalmoscopically the retinal arteries were clearly seen to be narrowed when the local asphyxia was at its height, and these vessels *became widened at the moment when reaction set in.*

Raynaud attributed these ocular phenomena to spasmodic contraction of the retinal arteries.

A case of recurrent temporary amblyopia recorded by the late Dr. C. E. Beevor and Mr. R. Marcus Gunn† and attributed by them to recurrent spasm of the arteria centralis retinæ is of unusual interest. The patient was a man, æt. 34 years. From the age of seven he had been liable to attacks in which he became suddenly blind for a few minutes, the loss of sight affecting especially the right eye. During these attacks he saw brownish discs and zigzags without colour, and they were not associated with headache. Finally after a severe attack he permanently lost the upper half of the field of vision of the right eye. Subsequently to this he had several attacks, in each of which there was total blindness of the right eye.

* Raynaud, *loc. cit.*, p. 164.

† 'Trans. of Ophthal. Soc. of the United Kingdom,' 1899, vol. xix, p. 75.

"Independently of these attacks he has had at times, ever since he was at school, curious feelings of being tired and dreamy, lasting a few seconds. In these dreamy attacks he does not lose his senses, but he does not quite remember why he is in a certain place, occurring events do not seem natural, and he has the idea of some impending calamity. They occur sometimes after the attacks of blindness."

On ophthalmoscopic examination in the right eye the optic disc is pale in its lower half and there is evident shrinking of the lower half of the arteria centralis retinæ. The upper vessels and the lower veins look normal. On one occasion a similar attack affected the left eye.

Finally, two months before coming under observation he had an attack "in which he described the symptoms as coldness and numbness in the hands and feet, followed by tonic spasm of the limbs and then by general twitching, but without loss of consciousness." Further, this patient's sister was liable to attacks in which "she has a feeling of contraction, or sometimes sharp pain, at the back of the right eye, and objects appear to recede from her and to get smaller, and finally to disappear in a white fog for a few minutes; the objects then rearrange themselves, and in from ten to fifteen minutes from the commencement of the attack they return to their normal appearance." She was also subject to attacks of ordinary migraine apart from the attacks just described.

Beevor and Gunn also quote a case of Benson's, of Dublin, in which similar recurrent attacks of amblyopia occurred, and in which Benson had the opportunity of examining the fundus during an attack: "The largest division of the inferior temporal artery of the retina was entirely bloodless for about four O.D. diameters of its length, while the other vessels seemed normal. In a few seconds a change occurred, the anæmic portion of the vessels seemed to change its position and moved towards the periphery of the fundus, at times slowly and steadily, and at other times in less regular progression, till it reached the next largest bifurcation, when it suddenly disappeared completely, leaving the whole fundus exactly as he was accustomed to see it."

In the discussion following the paper, Dr. Priestley Smith mentioned a similar case in a lady associated with attacks of ovarian pain and faintness.

The importance of Beevor and Gunn's case can hardly be over-estimated. The neuropathic relationship was shown by the presence of similar attacks and of migraine in the patient's sister.

When we review the symptoms we notice, first, the single attack, in which there was marked vasomotor change in the peripheral vessels as evidenced by coldness, numbness and spasm of the limbs, an attack which may be compared with those described in detail in the last lecture; secondly, recurring attacks of amblyopia, attributed by Beevor and

Gunn to spasm of retinal artery. Unfortunately the fundus was not examined in an attack, but in the exactly similar case described by Benson the opportunity presented itself and the spasm was actually seen. Compare also the similar appearances noted by Raynaud in his cases of amblyopia in Raynaud's disease. Lastly there were attacks of dreamy state, so frequently observed in *petit mal*, sometimes occurring after the attacks of blindness. Is any other conclusion open to us other than that the dreamy state was similarly due to arterial spasm in the brain? Such spasm we are of course unable to see, nor do we know the position in the brain which would correspond to the state; but short of actually seeing it the evidence seems conclusive that such must have occurred.

Pal* regards the transitory amaurosis of lead poisoning as being the result of a cerebral vascular crisis.

A most interesting case published by Thomas and Osler† shows the occurrence of epileptic convulsions with attacks of Raynaud's disease.

The sequence of events was as follows:—First, the fingers became cold, white and dead, and the nails blue, associated with considerable pain. Then followed general chilliness, with cold feet. These premonitory symptoms lasted for five

* Pal, 'Centrabl. f. Inn. Med.,' 1903, vol. xxiv, p. 417.

† "A Case of Raynaud's Disease associated with Convulsions and Hæmoglobinuria," 'Johns Hopkins Hosp. Rep.,' 1891, p. 114.

minutes, and were succeeded by unconsciousness and convulsions lasting for half an hour. In this case there was, first, the arterial spasm leading to the local syncope of the fingers; and secondly, general chilliness, probably to be attributed to a general cutaneous vaso-constriction.

It seems reasonable to assume that the convulsions were the result of vaso-constriction affecting the cerebral vessels, and it is very interesting to note that Raynaud's disease is apt to be associated with epileptic fits. According to Monro* 5 per cent. of the cases of Raynaud's disease have suffered from convulsions at some time or other.

In another case of Raynaud's disease recorded by Osler† recurrent attacks of hemiplegia and aphasia occurred. The patient was a woman subject to occasional attacks of local asphyxia. In April, 1891, she had her first cerebral attack, comprising dizziness and transient obscuration of consciousness; two similar attacks occurred in the next ten months. During the course of the next four years she had three attacks of aphasia with partial right hemiplegia and one of left-sided weakness. These attacks occurred concurrently with local arterial trouble of fingers and hand. Finally, in January, 1896, there was a severe attack with gangrene of right hand; no aphasia occurred,

* 'Raynaud's Disease,' 1899, p. 151.

† "The Cerebral Complications of Raynaud's Disease," 'Amer. Journ. of Med. Sci.,' 1896, vol. cxii, p. 522.

but she became comatose and died in a couple of days. No post-mortem examination.

The identity of the pathological process underlying the cerebral attacks and the local syncope and gangrene can hardly be called in question. The terminal coma is interesting; the possibility of its being due to cerebral œdema must be considered. The hemiplegic attacks might be due to arterial spasm or œdema, for, as already mentioned, these two phenomena seem to be almost interchangeable in Raynaud's disease.

Migraine.

The association of epilepsy with migraine is of considerable interest. It occasionally happens that periodical attacks of migraine are replaced by ordinary epilepsy, the migraine then ceasing. In migraine there is undoubted evidence of abnormal vaso-motor action. Chilliness of the skin is common: the temporal artery on the affected side is often contracted and hard. Relief of the pain often attends compression of the carotid artery. This, and the fact that the pain in the head is of a throbbing character, suggest that the old explanation of the vaso-dilatation of the cerebral vessels is correct. Such a dilatation of the vessels, with resultant increased tension of the dura, etc., would be enough to account for the pain. The brain tissue itself is insensitive, and Harvey Cushing has noted that after excision of the Gasserian ganglion any subsequent headache is only felt on the side

with the intact fifth nerve, an observation which indicates that intra-cranial pain is experienced *via* the branches of the fifth nerve to the dura and membranes of the brain. The dilatation can, moreover, be seen. Thus Mollendorff* points out that "during the attacks the background of the eye on the suffering side was of a bright scarlet red, the optic papilla red and œdematous, the arteria and vena centralis retinæ enlarged, the latter knotty and very tortuous." There is much to be said for the view that the symptoms of migraine depend upon abnormal vaso-motor activity, and that the headache is the result of vaso-dilatation.

Gowers† records the following cases :

In one, a woman, æt. 38 years, had been subject to migraine from the age of six. For many years when the pain was most intense she suddenly felt a peculiar sensation at the epigastrium, which passed up through the chest to the head, and seemed to spread over the whole head. It continued for ten minutes, and ended as suddenly as it began with an eructation of flatus. During the sensation she was unable to see, or to speak, or to understand what was said to her. She heard words as sounds but could not tell their meaning. When the sensation ended sight returned, and her power of speech came back gradually ; at first

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* See Liveing, 'Megrim and Sick Headache' 1873, p. 307.

† 'Borderland of Epilepsy,' p. 93.

on trying to say a word she could not utter it correctly. At the age of thirty-three this sudden state became a definite epileptic fit. When the headache reached its height she lost consciousness ; general convulsion occurred, with tongue-biting and micturition. These fits became her chief trouble and they always occurred during the course of the headache.

The epigastric sensation, so common an aura in epilepsy, was discussed in the last lecture, and it was suggested that it was due to a sudden splanchnic dilatation. The condition of the patient after it occurred was very similar to some of the cases of so-called vagal or vaso-vagal attacks. The replacement of this state by an epileptic fit may be explained by a more sudden splanchnic dilatation or by a severe cardiac inhibition concurrent with the splanchnic dilatation.

In another the patient was a girl, æt. 16 years, who had been subject to periodical attacks of migraine since the age of five years. At thirteen and a half she had an epileptic fit during sleep, and since then three others—two during sleep and one when awake. Since the first fit the headaches had been frequent, but were preceded by a brief but very definite visual aura. The interesting point is that the single epileptic fit which occurred when she was awake was preceded by precisely the same aura. An interpretation that is possible for this case is that local vaso-constriction was

responsible for the premonitory visual manifestation, and was succeeded by a local vaso-dilatation in the attacks of migraine, and either by a more severe and widespread cerebral vaso-constriction or by cardiac inhibition in the epileptic attack.

Migraine is also occasionally accompanied by transient aphasia. Conditions such as these suggest very strongly that abnormal vaso-motor phenomena are concerned and transient spasm of cerebral arteries is not an unreasonable hypothesis.

The evidence for the existence of vaso-motor activity in the brain is therefore partly direct and partly indirect. It is obviously a matter of great difficulty in clinical work to demonstrate such alterations, owing firstly to their evanescence, and secondly to the fact that when they have subsided no evidence of their existence is left behind.

Petit Mal.

A consideration of the cerebral phenomena attending cases of heart-block shows us that the attacks present an increasing degree of severity proportional to the length of the period of asystole. There may be merely a transient giddiness, a dazed feeling, a "turn," or the head may drop forward momentarily, the patient recovering himself immediately; or unconsciousness may be rather deeper though still transient; or a fall with slight spasm; or, finally, a severe general convulsion. Every one of these phases could be duplicated among

the numerous manifestations of minor and major epilepsy. And when we compare the gradually increasing severity of the manifestations, according to the length of the period of cardiac asystole, with the phenomena of epilepsy, the resemblance is more than suggestive.

Discussing the types and degrees of seizures, Aldren Turner* remarks that—

" . . . The primary types of epileptic attacks denote consecutive stages of the same series of phenomena—stages which may be arrested at any period."

Among various examples given by Turner is the following :

"A common form of incomplete attack is seen in fits, the aura of which is a feeling of giddiness followed by a sudden fall from loss of consciousness, but without convulsion. In these cases there are commonly found attacks of giddiness (aura), as well as complete seizures, in which the fall is followed by the usual convulsive phenomena of a major fit."

In other words, the stages of severity observed are, firstly, an attack of giddiness only ; secondly, an attack of giddiness followed by a fall ; and, finally, the complete fit, terminating in convulsions.

In a case of my own, a girl, A. L—, æt. 12 years, was subject to both major and minor attacks, the latter being described as attacks of giddiness. She has suffered from epilepsy since the age of six.

* ' Epilepsy,' 1907, p. 69.

On one occasion I was feeling her pulse. She was telling me of her state during the past fortnight and was saying that she was that day feeling perfectly well. She was not nervous at the time, but suddenly the pulse stopped; she gave a short cry, clutched at my coat, and sat down in a chair by which she had been standing. She did not lose consciousness. The cardiac arrest was of very short duration, probably about five seconds, and the heart then began to beat again, but the pulse was extremely feeble for a few contractions, perhaps from fifteen to twenty, and then rapidly increased in force so that within about half a minute from its reappearance it had regained its previous state. A few minutes later its rate was 124—a rate very common in this particular case. The above attack was a typical example of many of her minor seizures. She herself complained of giddiness and thought she was going to have a fit, as this sensation usually preceded a major attack, though an accompanying aura, a feeling of a desire to micturate, was absent. The child is always much frightened by these attacks.

Here was a case of cardiac inhibition in what would be called *petit mal*, but which I think would be more accurately described as an incomplete or abortive major attack. The cessation of pulse and the child's cry were, I think, simultaneous. Had the cardiac arrest been of longer duration a fully developed major attack would doubtless have occurred.

Again, in Finny's case of bradycardia recorded in the first lecture, the attacks varied from what were called "weak turns" to "slight fits" and "severe fits." The case was at first regarded as one of *petit mal.* It is very interesting to note that the slight fits came on with soreness or sharp feeling in the stomach and left side of the thorax, which would then extend up to the right side of the chest into the head and eyes—a definite aura in fact.

Here we have an aura, and if it had occurred in a case of idiopathic epilepsy it would have been regarded as typical, but it occurred in a patient whose attacks were unquestionably secondary to cerebral anæmia from heart block. Whether the aura was due to sensations derived from the peripheral vessels and heart, or to cerebral changes resulting from the cessation of the circulation, it is difficult to say, but there can be no doubt that it was of circulatory origin.

Finally, in the severe fit in the same patient the onset was more sudden; there were convulsive movements of limbs, and the patient came out of it very confused, and was dull and nervous the whole day following.

Such resemblances are too close to be due to mere coincidence. It is difficult to conceive of any other explanation than an identity of cause. The cause was unquestionably sudden failure of the cerebral circulation in the case described, and the conclusion seems inevitable that some attacks of *petit mal* are determined in a similar way.

But it cannot be claimed that cardiac inhibition occurs in all cases of minor epilepsy. Moxon* quotes Hughlings Jackson's observations of the disappearance of the pulse at the onset of attacks of *petit mal*. I myself was on two occasions feeling the pulse of a boy subject to minor attacks when one supervened. No arrest occurred nor was there any obvious change in the pulse-rate. Evidence has been adduced as to the occasional occurrence of transient spasm of the cerebral arteries, and such spasm may underlie these attacks. It is suggested, therefore, that two factors may be concerned in the production of *petit mal*. Some cases may be due to very transient cardiac failure and others to transient spasm of the cerebral arteries.

Infantile Convulsions.

The similarity between infantile convulsions and those of idiopathic epilepsy is so close that the probability of the same factor underlying the two conditions must be very considerable. The vaso-motor system of the child is much more unstable than that of the adult, and the ease with which emotional disturbance and shock are produced is notorious. In a considerable number of cases the occurrence of apparently ordinary infantile convulsions is the starting-point of chronic epilepsy; in other words, of the enormous numbers of children affected with infantile convulsions, some

* "On the Influence of the Circulation on the Nervous System," 'Lancet,' 1881, vol. i, p. 648.

become chronic epileptics while others do not. There is nothing in the type of the fits which enables us to determine whether chronic epilepsy is likely to follow or not.

It seems hardly open to doubt but that the large numbers of alleged causes of infantile convulsions, such as teething, rickets, worms, acute infections, gastro-intestinal disturbance, fright, and so on, must exert their influence *via* some common factor. Such a factor might be, as suggested, abnormal vaso-motor and cardio-motor systems with a ready liability to attacks of acute circulatory failure, either from cardiac inhibition or from splanchnic dilatation. If this factor is brought into play once only we have an isolated convulsion; if only a few times we have a few convulsions. If, however, it is brought into action over and over again, chronic epilepsy is the result.

Children are more susceptible to fear than adults. Discussing the effects of fright, J. R. Charles* remarks that:

"As regards the vaso-motor apparatus, there is widespread vaso-motor constriction of the cutaneous area, with a feeling of chilliness, shivering, and goose-skin. At the same time there is probably a corresponding vaso-dilatation of some of the internal vessels, as evidenced by the copious secretion of urine, and also by diarrhœa. As a rule the heart beats quickly and violently, but if

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* 'Bristol Med.-Chir. Journ.,' 1906, vol. xxiv, p. 23.

the impression is very sudden and intense there may be *complete arrest of the heart's action.* There is frequently a spasm of some of the involuntary muscles, leading to involuntary micturition and less frequently defæcation, and a feeling of oppression and constriction in the chest, possibly due to contraction of the bronchial muscles. . . . Tremor is so common that the verb 'to tremble' has become almost synonymous with the verb 'to fear.' . . . More rarely the muscles may become rigid, or be *thrown into convulsive movements during moments of great terror.* . . . It will be noticed that there are certain points of analogy between the bodily effects of fright and those of cold, viz. the cold surface from vaso-motor constriction, the goose-skin, erection of hair, polyuria, tendency to diarrhœa, and tremor."

Speaking of the influence of mental emotion as an excitant of epilepsy, Gowers* states :

"Of all the immediate causes of epilepsy the most potent are psychical—fright, excitement, anxiety. To these were ascribed more than one third of those in which a definite cause was given. Of the three forms of emotion fright takes the first place. It is effective chiefly in early life, when emotion is so readily excited, and is most powerful at the transition from childhood to adult life, while after middle life it is almost inactive. . . . The female sex is notoriously the

* 'Epilepsy,' second edition, p. 25.

more emotional, and accordingly the disease results from fright in a larger proportion of females than of males. . . . It is also notorious that this difference between the sexes increases as life advances. In childhood one sex is almost as emotional as the other, but with puberty men become far less emotional than women. The influence of fright as a cause of epilepsy is in strict harmony with this fact. Under ten years of age the sexes suffer equally. Between ten and twenty the males suffer less than females, as 3 to 4; between twenty and thirty as 3 to 13; and over thirty the only cases due to this cause occurred in women."

When we reflect on the above remarks on the influence of fright in producing epilepsy, and on the fact that fright exerts a great influence on the cardiac and vaso-motor systems, and that a severe fright can cause a transient stoppage of the heart and even death, the evidence points strongly in the direction that the convulsions of infancy must depend on an affection of the cardiac and vaso-motor systems, and that the immediate factor in the attack is either a cardiac arrest or a cardiac failure so severe as to give rise to rapid failure in the cerebral circulation.

The convulsions met with at the onset of acute infections in childhood are worthy of mention. Under similar conditions rigors are common in the adult, so much so that it is almost an aphorism that a convulsion in a child is the equivalent of a rigor in an adult. I have, however, once seen a

convulsion at the onset of pneumonia in a non-epileptic adult.

A rigor is associated with marked cutaneous vaso-constriction, with pallor and sensation of great cold. The sensitive cardiac and vaso-motor systems of the child may not be able to adjust themselves to a severe vascular crisis, and it is to be noted that the old-established method of cutting short convulsions in infancy by means of immersion in a warm bath by producing vaso-dilatation of the skin lowers the blood-pressure and relieves the heart.

Jacksonian Convulsions.

Local stimulation of the cerebral cortex by the electric current, or by the presence of a cortical tumour, are both competent to produce that type of convulsive seizure commonly known as Jacksonian. The muscles first involved in the convulsive movements are those related to the area stimulated, but the spasms rapidly spread to other groups, and finally the whole musculature of the body may be involved. Consciousness is not always lost in these fits, and if lost, only late in the course of the fit. The spread of the convulsion to muscles other than those related to the area stimulated indicates that a progressively increasing area of cortex becomes involved. Several possible explanations of this march of events must be considered.

(1) It might be due to a spread of the current; but if so one would expect that the spread should

occur at the moment of application of the current, and moreover, the fact that areas very remote from the one primarily stimulated are involved—for instance, the opposite side of the brain—renders such an explanation very improbable.

(2) To a spread of the excitation, the view commonly held. That the area of musculature involved in the convulsive movements gradually widens is proof that the excitation spreads, but it affords no explanation as to *how* it spreads.

(3) It might be due to a spreading vaso-con striction of the cerebral blood-vessels, the resulting anæmia bringing about the spread of the convulsions. I have referred above to evidence suggesting that the cerebral vaso-motor mechanism is a much more active one than is generally assumed, and I would draw attention again to Harvey Cushing's observation that faradic stimulation of the cortex can produce a paling of the grey matter. It might be urged that if this were of common occurrence it should have often been observed, but it might easily be overlooked, for slight paling of a surface is not a very obvious alteration.

Sir Victor Horsley* was on one occasion operating on the cortex when the patient had an epileptic fit. He noted that the cortex became distinctly *hyperæmic during* the attack. This it would do as the result of the convulsions forcing

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* Horsley, "Origin and Seat of Epileptic Disturbances," 'Brit. Med. Journ.,' 1892, vol. i, p. 693.

blood upwards through the great veins of the neck into the brain. The increasing venosity of the blood would also deepen the colour of the cortex, and moreover attention would in all probability not be attracted by any paling of the cortex but by the convulsions, when hyperæmia would occur almost immediately.

The phenomena of Jacksonian fits dependent on tumour might be susceptible of the same explanation, viz. a spreading vaso-constriction; but it is certainly difficult to correlate them with cerebral anæmia, and the possibility that they depend on a different mechanism must be admitted.

The Symptoms following upon Sudden and Prolonged Cerebral Anæmia.

So far we have considered the results following sudden and very transient cerebral anæmia. The symptoms resulting from a more prolonged arrest of the cerebral circulation are not less interesting. I have recorded two cases in which death occurred three and five days respectively after puncture of the chest. I will briefly note the salient features of these two cases:

Case 1. *Broncho-pneumonia and pulmonary collapse; exploration of lung with hypodermic syringe; collapse and convulsions; death five days later.*—F. J. S—, female, æt. 7 years, admitted into St. Thomas's Hospital March 7th, died March 13th, 1898.

On March 8th, at 11.30 a.m., an exploring

needle was inserted into the right base. During the exploration the child lost consciousness, was stated to become very pale on the right side of the face, and also slightly cyanosed. Ether was injected subcutaneously and stimulants administered. At 1.30 p.m. she had a convulsion, and convulsions occurred frequently during the afternoon.

On March 9th her pulse was 132 and weak, head retracted, and she was still practically comatose.

By the eleventh the retraction of head had almost disappeared; she was irritable, resented all interference, and passed her evacuations into the bed. She remained unconscious and died on March 13th.

Post mortem.—The special feature of the appearance of the brain was its vascularity. There were a few small superficial hæmorrhages in the pia mater and the vessels over both hemispheres were much injected. On section the white matter had a pinkish colour, and there were numerous red spots where vessels had been cut across. The lateral ventricles were undistended and contained no excess of fluid. The vessels at the base and in the Sylvian fissures were healthy.

Case 2. *Old pulmonary tuberculosis; chronic left basal pneumonia; exploratory puncture; syncope, convulsions, left hemiplegia; death three days later.*—J. R.—, male, æt. 52 years, under the care of Dr. Acland at Brompton Hospital; admitted June 14th died June 17th, 1890.

On examination the physical signs were suggestive of a localised collection of fluid at the left base. A puncture was therefore made just under the angle of the scapula. The needle was inserted for about an inch and a half, and seemed to penetrate a solid substance; no fluid being withdrawn, a second puncture was made one intercostal space lower. On asking the patient if it gave him any pain he replied quite naturally, "I hardly felt it;" he then almost immediately passed a large quantity of urine, turned pale, and fell backwards. Respiration ceased entirely at once; the heart beat most irregularly and spasmodically, and the radial pulse was not to be felt. Ether was injected subcutaneously, the interrupted current was applied, and artificial respiration was maintained for half an hour. He then had a fit in which the left arm became firmly flexed at the elbow, the thumb flexed into the palm, the fingers over the thumb, and the hand flexed at the wrist. The left leg was not affected. The eyes were deviated to the right and the pupils widely dilated. When examined a few hours later he was still unconscious. The left side of his face was slightly less wrinkled than the right; the left arm at times moved slightly, and then would become rigid and flexed; the left leg was rigid, the knee-jerk was exaggerated, and ankle-clonus was obtained with difficulty. The right arm was moved up and down occasionally.

On the morning of June 15th his pulse was 150. There was now obvious left hemiplegia, with much

twitching of the muscles of the left side of the thorax and abdomen. In the evening the right arm was rigid and flexed, the right leg was extended and constantly twitching; ankle-clonus was obtained on both sides—more briskly on the right. The urine contained a trace of albumen.

On the morning of June 16th he was still unconscious. The left hemiplegia still persisted; the right arm was rigid with clonic spasms; ankle-clonus was absent, and the knee-jerk could not be elicited on either side. Several convulsive seizures occurred during the evening. The left optic disc was apparently swollen and blurred, with one flame-coloured patch; the right cornea was hazy, and the disc looked blurred. Death occurred three days after the onset.

Post mortem.—The pia mater generally was slightly opaque. The dura also was slightly thickened, but there were no morbid adhesions. The vessels at the base of the brain were healthy. The brain tissue was fairly firm, and no obvious lesion could be detected in any part.

It is unfortunate that no microscopical examination of the brain was made in either case.

In a case recorded by Hubert Armstrong,* the initial symptoms were those of complete cardiac inhibition, but recovery occurred in a few hours.

Several cases presenting similar features are on

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* 'Liverpool Med.-Chir. Journ.,' July, 1906, p. 110.

record in which the symptoms followed pleural lavage.

Dr. Cayley* reports one in which death occurred from washing out the pleura after operation for empyema. On one occasion the patient "became deadly pale, his arms stiffened, and his pulse became very slow, his pupils were widely dilated, and his breathing gasping. . . . The patient, who was profoundly unconscious, now became flushed, his pulse and breathing extremely rapid; he had convulsive tremors of the right arm and leg, the hand was clenched and the arm rigidly flexed; the left limbs were also rigid and extended. The head was sometimes turned to the right, sometimes to the left; the eyelids were closed, the eyeballs were constantly rolling from side to side, and there were spasmodic twitchings of the muscles of the right side of the face. The pupils were widely dilated and insensitive to light; the patient's body became bathed in a profuse sweat, and the tempera ture rose rapidly. . . . He remained unconscious with general convulsive twitchings, and died sixteen hours after the seizure."

Post mortem.—"The brain and its membranes appeared quite normal; no thrombosis or embolism of the sinuses or arteries could be discovered. Portions of the medulla were submitted to microscopical examination but nothing abnormal was discovered."

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* Cayley, 'Clin. Soc. Trans.,' vol. x, 1877, p. 16.

Dr. Goodhart* records a similar case in which death occurred nine hours after onset. A girl, æt. 16 years, was operated on for empyema, and the pleura washed out daily. On one occasion she suddenly turned livid and fell back. She ceased to breathe and no pulse could be found at the wrist; no convulsive fit occurred. Artificial respiration was immediately commenced, and in ten minutes respiration was re-established and the pulse could be felt feebly at the wrist. She was perfectly insensible and never recovered consciousness in the slightest degree. An hour after the attack the right side of the face and the right arm and hand were very blue and congested; this subsequently disappeared. Urine and fæces were discharged involuntarily soon after the attack commenced. Both arms were contracted and rigid. There was no paralysis or rigidity of legs. Transient paralysis of the right side of the face occurred. Both arms were moved about alternately. Death occurred nine hours after the onset.

Post mortem.—The brain and spinal cord were found to be quite healthy. The membranes, sinuses and vessels were searched without finding any evidence of thrombosis or embolism.

Raynaud describes a similar case† of a man,

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* "Empyema and its Treatment," 'Guy's Hospital Reports,' 1877.

† "De la mort subite dans la thoracentèse et des convulsions epileptiformes à la suite des injections pleurales,' Gaz. des Hôp.,' 1875, p. 1068.

æt. 27 years, in whom daily lavage of the pleura was being carried out for empyema. On one occasion the patient collapsed, became extremely pale, with convulsive movements of arms; he scarcely breathed, and the pulse was feeble and intermittent. After recovery in half an hour vision was obscured. The right papilla was surrounded by serous effusion, the veins were in some places much swollen, in others compressed and empty. The inner half of the disc was of a dull white colour, and the outer red and with blurred edge. On the left side the disc was pale. By the evening consciousness had returned but sight remained abolished.

On the same evening another lavage was performed but was again followed by an epileptic fit—severer than the first—and this was succedeed by a state of stertor absolutely similar to that of ordinary epilepsy. This lasted several hours, and then a series of epileptic fits occurred terminating in death.

Post mortem.—Nothing abnormal was found in the brain. Further, the patient had never suffered from any convulsion before.

Raynaud regarded these cases as not being epileptic (idiopathic) but as being due to the injection into the pleura, and attributed the syncope to a reflex vagus cardiac arrest, or to a reflex cerebral vaso-motor constriction involving the medulla.

Vallin* records the case of a man, æt. 23 years,

* "Convulsions éclamptiques à la suite de la thoracentèse," Vallin, 'Gaz. des Hôp.,' 1875, p. 1116.

with daily irrigations for empyema. On one occasion, and at the end of the lavage, sudden syncope occurred. Rigidity of limbs, coldness of extremities, and cyanosis of face were present. After three quarters of an hour opisthotonos. Death twelve hours later without recovery of consciousness. Post mortem *nil*.

Cayley further quotes a case of Lorey's in which after recovery of consciousness the ocular fundi were examined; the retinal arteries were found to be much reduced in calibre, the veins in part dilated and congested. In this particular case a further washing out of the pleura was followed by convulsions and death as in the above cases.

Post mortem.—Nothing was found in the brain to account for the condition.

The condition is fully described by Bouveret* who gives a full *resumé* of all cases up to 1888.

The causation of the cardiac arrest in these cases is of great interest. In some experiments† performed in conjunction with Professor Brodie, with the object of ascertaining which of the afferent fibres of the vagus cause inhibition of the heart when their central ends are excited, we found that the pulmonary fibres were by far the most effective in this respect. If the root of the lung be exposed in an animal and any of the pulmonary branches stimulated, a typical arrest of the ven-

* 'Traité de l'Empyème,' Paris, 1888.

† "On Reflex Cardiac Inhibition," 'Journ. of Physiol.,' 1900, vol. xxvi, p. 92.

tricular contraction, as shown by the blood-pressure record, is produced. At the same time marked arrest of respiration occurs from excitation of the respiratory centre. The vaso-motor centre is also inhibited, and produces a further fall in blood-pressure, apart from that due to the cardiac inhibition, as proved by the fall in blood-pressure produced in an animal whose cardio-inhibitory fibres have been paralysed by atropine.

The subject has also been studied by Capps and Lewis* who concluded from experiments on animals with artificially induced pleurisy and from observations on the blood-pressure of man during aspiration of pleural effusions, that the pleural fibres of the vagus can give rise to a very active lowering of blood-pressure, and that this may be brought about either from a reflex vaso-motor depression or a reflex cardiac inhibition.

Similar Symptoms resulting from Prolonged Chloroform Syncope.

The conclusion that the cerebral manifestations in the above cases are due to prolonged cerebral anæmia is supported by the facts published by T. A. Green in his paper on "Heart Massage as a Means of Restoration in Cases of Apparent Sudden

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* J. A. Capps and D. D. Lewis, "Observations upon Certain Blood-Pressure Lowering Reflexes that arise from Irritation of the Inflamed Pleura," 'Amer. Journ. of Med. Sci.,' 1907, vol. cxxxiv, p. 890.

Death."* Numerous cases of recovery after chloroform syncope as the result of massage of the heart are on record, but in some, although the heart has been induced to beat apparently normally, death has resulted after a varying period with a train of symptoms indistinguishable from those noted in the above cases. The fact that in these cases of chloroform syncope the heart had ceased to beat for varying periods, and that therefore the cerebral circulation was for a time at a complete standstill, leaves no room for doubt but that the cerebral symptoms are to be attributed to the cessation of the blood-flow through the cerebral arteries.

Green's first case is as follows :

A boy, æt. 9 years, was being operated on for congenital umbilical fistula. During the early stage of the operation respiration stopped, "the lips became cyanosed, the skin pale and the pupils of the eyes widely dilated and insensitive. No pulse could be felt at the wrist and on auscultation no heart-sounds could be heard. The respiration continued spasmodically at intervals but finally stopped about five minutes later." All the ordinary means of restoration having failed, twenty-five minutes after the cardiac stoppage Dr. Green opened the abdomen under the left costal arch and commenced cardiac massage through the diaphragm. The apex of the heart was felt to be quite immobile and flaccid. Rhythmical com-

* 'Lancet,' December 22nd, 1906.

pression of the heart was practised at a rate of about 70 per minute. After about two minutes a slight fluttering of the heart was observed and at the same time the pupils contracted slightly. Within a few seconds it began to beat with more than normal vigour at a rate of about 90 or 100 per minute. Artificial respiration had been continued all the time, and within a very short time of the restoration of the pulse spontaneous breathing asserted itself. Consciousness never returned, tonic spasms with rigidity of the limbs and trunk developed; he broke out into severe perspirations and the pulse and respirations increased in frequency. The muscular spasms were severe enough to necessitate the administration of morphia and chloroform. Death occurred twenty hours after the heart-beat and respiration had been re-established.

Green also records a second but less striking case occurring under his own observation, in which death occurred one and a half hours after the heart massage had been commenced.

Green reviews the literature and gives a synopsis of forty cases of heart massage for chloroform syncope, but for the purposes of this paper only those in which death occurred some hours after the heart failure will be mentioned.

Maag.* A man, æt. 27 years. Operation, nerve-stretching for sciatica. The patient became

* 'Centralbl. f. Chir.,' 1901, p. 20.

"asphyxiated" at the end of the operation. Ordinary measures tried for ten to fifteen minutes. The heart was exposed by the thoracic route, the third and fourth ribs being divided. Tracheotomy was performed and air blown into the lungs.

After a few compressions the heart began to beat, at first feebly, then more firmly. At the end of half an hour the first natural respiration was taken, but it was not until the end of three hours that these were deep and regular. Consciousness was never recovered, and the patient died eleven hours after the cardiac action had been re-established. During the last eight hours voluntary respiration was absent.

Gray.* Operation on a woman, æt. 55 years, for sudden asphyxia from laryngeal carcinoma. Tracheotomy was performed with artificial respiration. A few spontaneous respirations were taken but they soon ceased. After four or five minutes the abdomen was opened and the heart massaged through the diaphragm. It began to beat after four minutes, slowly at first, but gradually increasing in rate and strength up to 90 per minute. Artificial respiration was continued and gradually natural breathing was restored. Consciousness was never regained and the patient died three hours later. Cardiac arrest lasted about ten minutes.

Depage.† Woman; abdominal hysterectomy

* 'Lancet,' August 19th, 1905, p. 506.

† Depage, 'Journal de Chirurgie et Annales de la Société Belge de Chirurgie,' 1905, p. 238.

for fibroid. Chloroform syncope. Artificial respiration for fifteen minutes; then heart massage by the subdiaphragmatic route. The heart-beat was restored in a few instants; it was feeble at first but it soon became stronger. Spontaneous respiration did not return until one hour had elapsed. Consciousness was never recovered and she died after sixteen hours.

Ramsay.* Woman, æt. 27 years. Operation for prolapse of uterus. Chloroform syncope. Artificial respiration was commenced immediately. At the end of four minutes heart massage by the subdiaphragmatic route. Pulsation returned within a minute, at first feebly then becoming stronger, and spontaneous breathing soon followed. Three hours later the pulse was 168, irregular and intermittent. She slept for four hours and was at times delirious. On the next day she was better and she made a good recovery.

I have thought it advisable to mention in some detail the results following complete and prolonged cerebral anæmia, as though they have been described in the case of experimental ligation of the cerebral arteries in animals, they are not generally recognised as occurring in clinical medicine. In the next lecture I will continue this part of the subject, and also deal with conditions dependent upon increased intra-cranial tension with its resultant cerebral anæmia.

* Ramsay, 'Intercolonial Medical Journal of Australasia,' September, 1906.

LECTURE III.

Mr. President and Gentlemen,—In the last lecture we were considering the clinical symptoms following upon prolonged cessation of the blood-flow through the brain, as found in cases of cardiac syncope following exploratory puncture of the lung and lavage of the pleural cavity, and in cases of chloroform syncope in which the cardiac action had been restored by direct massage of the heart after prolonged arrest.

The subject has been studied experimentally by various observers. The blood supply to the brain of animals has been cut off and the effects produced on allowing the circulation to return have been studied. One of the most exhaustive studies has been made by Messrs. Stewart, Guthrie, Burns and Pike.* Their experiments were performed on cats. The animals were anæsthetised with ether; ligatures were placed round the innominate and the left subclavian artery proximal to the origin of the vertebral artery, the blood-flow being stopped by traction on the ligatures. Artificial respiration was kept up.

* "The Resuscitation of the Central Nervous System of Mammals," by G. N. Stewart, C. C. Guthrie, R. L. Burns, and F. H. Pike, 'Journ. of Exp. Med.,' 1906, vol. viii, p. 289.

The extent of anæmia was tested by means of intra-venous injections of indigo-carmine in animals allowed to die without restoration of the cerebral circulation. It was found that anæmia of the brain and medulla was complete; no trace of pigment was ever found above the calamus scriptorius and usually none above the third or fourth cervical vertebra.

There is, however, an important distinction between their experiments and the results obtaining in the cases described in the last lecture. In the experiments the blood-flow was cut off from the brain and medulla only, the circulation in the greater part of the cord and in the trunk and lower extremities remaining; whereas in the clinical cases the whole circulation of necessity came to an end.

The observers noted the effects produced on the blood-pressure, pulse-rate, respiration, reflexes and muscular movements.

The light, lid and corneal reflexes vanished almost immediately after occlusion. The pupils dilated in from ten to sixty seconds. When dilatation began it rapidly developed, the maximal dilatation being attained in from four to five seconds. Then the cornea became lax, sunken and furrowed, indicating the reduced intra-cranial pressure.

Muscular movements.—There was usually a sudden stiffening of all the muscles following occlusion, with violent movements of fore and

hind limbs and tail. Micturition and defæcation might occur. Then the fore-limb movements ceased; shortly afterwards the hind limbs relaxed, and the whole animal lay limp and quiet until after the restoration of the cerebral circulation. Intra-venous injection of strychnine during occlusion caused spasms of abdominal muscles and of hind limbs, but not of fore limbs, indicating that the anterior part of the cord had been rendered anæmic.

The cerebral circulation was allowed to return after varying periods and the effects noted.

Respiration.—The first sign of returning vitality in the respiratory centre was a strong gasp. This was repeated at progressively shorter intervals until spontaneous breathing was established. The first gasp might occur at a long interval after the restoration of the circulation. Thus, after an occlusion of twenty-eight minutes the first gasp occurred forty minutes after release.

The return of the reflexes was inconstant; thus the light reflex might not return for two or three days.

Convulsions.—"Convulsions varying in severity from occasional twitchings of the limbs to extreme opisthotonos and violent struggles of tonic or clonic type sometimes begin before the full return of the reflexes. Occasionally the cat may lie quiet for one to three hours before the convulsions begin. The head may be drawn back in extreme opisthotonos or may be bent downwards with the back convex.

There may be tonic spasm of the fore limbs and clonic spasms of the hind limbs. Again there may be violent clonic spasms in which the animal flings itself about from one side of the room to the other. The convulsions may follow in such rapid succession as to make it difficult to distinguish any interval between successive seizures. At other times intervals of five to twenty minutes elapse between any two convulsions. The pupils dilate widely between the spasms. Stroking the fur, clapping the hands together near the animal's ear, etc., may throw the animal into spasms. The period of frequent and violent spasms lasts from two or three hours to as many days." Severe convulsions may terminate in death twelve to thirty hours after their onset.

Transection of cord.—Division of the cord in the upper dorsal region between the third and sixth dorsal vertebræ, if done before fairly complete recovery of the cerebral centres, is followed by collapse, cessation of respiration, cardiac failure and death. The integrity of the spinal centres is necessary for the resuscitation of the cerebral centres. Division of the cord after the spasms are well established is followed by transient shock, recovery and cessation of the spasms in the hind limbs; hemisection produces cessation of the spasms in the hind limb of the same side.

After the convulsive stage is over the animals may recover completely or they may partially recover, but with loss of intelligence, dying after a variable period.

The Deportment of the Animal in the Post-Convulsive Stage.

(a) *Complete recovery* has occurred after occlusion of 5, 6, 8, 9, and 16½ minutes.

(b) *Partial recovery.*—One animal after occlusion of ten minutes recovered with loss of intelligence, the life of reflexes alone persisting. It had to be killed on the fifteenth day on account of puerperal infection. The convulsive movements persisted for three and a half days.

On the fourth day it could assume a half-sitting posture.

Sixth day: Walked clumsily, cleaned its paws, purred when stroked, took food for the first time, having been fed by the tube prior to this.

Seventh day: Walked in a circle, bumping against things.

Twelfth day: Four kittens born, paid no attention to them unless one was put near her, when she would fondle and lick it.

Fourteenth day: Seemed blind and deaf.

In another animal eight minutes' occlusion was followed by paralysis of one fore limb. There were occasional convulsions following violent attempts to move about in the later period. There was no loss of intelligence. Death on ninth day from accidental strangulation.

In another twenty-two minutes' occlusion; paralysis of one fore limb but no loss of intelligence; death from pneumonia on seventh day.

After long occlusion death usually followed in

thirty hours or less, and in these cases no post-convulsive stage was observed.

The Time Limit of the Recovery of the Brain from Arrest of the Circulation.

In the experiments on cats no animal recovered after a longer period of occlusion than 16½ minutes, though in one case after 22 minutes' occlusion the animal recovered without loss of intelligence but with paralysis of one fore limb, death following, however, from pneumonia on the seventh day. But these experiments did not impose so severe a test as in cardiac inhibition in man—for the heart remained beating during the whole period of occlusion of the cerebral arteries, so that the life of the spinal cord and of the rest of the body was not interfered with. The integrity of the spinal cord was found essential to recovery, transection in the upper dorsal region being incompatible with the resuscitation of the cerebral centres. In the cases recorded in man the spinal cord suffered from the same arrest of blood supply as the brain, and though this might not be so severe an injury as transection, it would presumably materially diminish the chances of recovery. It is difficult to say for what period the brain can withstand the total arrest of its blood supply and the patient make a complete recovery.

The following table taken from Green gives details of nine cases in which recovery followed direct massage of the heart for chloroform syncope :

Case.	Time of ordinary methods of resuscitation.	Time of restoration of heart from commencement of massage.	Time of restoration of breathing from commencement of massage.
Igelsrud	3–4 minutes	1 minute	—
Lane	Uncertain	1 or 2 squeezes	12 minutes
Gray	Uncertain	2 or 3 squeezes	—
Cohen	2 minutes	1 minute	—
Crile	His special methods commenced immediately	5 or 6 minutes	5 or 6 minutes
Sencert	7–8 minutes	5 minutes	7 minutes
Conkling	2 minutes	1 minute	—
Smith	3 minutes	1 minute	A few seconds after heart-beat had been restored
Ramsay	4 minutes	1 minute	Soon after heart-beat had been restored

In a case recorded by Sencert, seven or eight minutes is recorded as the time during which the heart was completely arrested before direct cardiac massage was commenced. A disaster such as chloroform syncope is not conducive to accurate observations of time, and it is probable that the heart gave some beats under the artificial respiration, etc., applied during this period; but it was motionless when massage was begun, and five minutes elapsed before its contractility was restored. Some blood would presumably be forced round the circulatory system during this five minutes, so that the full five minutes could not be added to the seven or eight.

In Ramsay's case four minutes elapsed between the cessation of the heart and the institution of cardiac massage, the heart recommencing to beat one minute later.

We are probably safe in assuming that about five minutes' loss of its circulation is the outside limit of time that the human brain can withstand and recover completely. In the experiments on cats, death without any return of reflexes followed an occlusion of $7\frac{1}{2}$ minutes, the longest period of occlusion with recovery being $16\frac{1}{2}$ minutes, and in all probability the cat would be more likely to recover after longer occlusion than man; further, as stated, the cats had the advantage that the circulation through the rest of the body and spinal cord was intact.

The heart itself even in man can of course withstand much longer periods of arrest and recover its contractility. This is shown in the next table, also taken from Green.

The longest duration of survival in these cases was in Green's patient, who lived for twenty hours. In the cases of surgical operations with chloroform syncope the patient has been exposed not only to the action of chloroform and a surgical operation of varying length, but also to a second abdominal operation for the purposes of carrying out the cardiac message, so that there are more factors against recovery than in the cases quoted of simple puncture of chest wall, and these cases survived for three and five days respectively.

Giving Particulars of Eight Cases in which Heart Massage was Partially Successful.

Case.	Time of ordinary methods of resuscitation.	Time of restoration of heart from commencement of massage.	Time of restoration of breathing from commencement of massage.	Survival.
Maag	10-15 minutes	A few compressions	3 hours	*
Sick	45 minutes	30 minutes	30 minutes	24 hours
Crile	*Nil*	9 minutes (Crile's special methods)	12 minutes	2 hours
Crile	*Nil*, but at least 8 minutes elapsed without any attempts	16 minutes (Crile's special methods)	16 minutes	34 minutes
Gray	4–5 minutes	4 minutes	4 minutes	2 hours
De-page	15 minutes	A few instants	1 hour	16 hours
Lenormant	*Nil*	6–8 minutes	¾ hour	5 hours
Green	25 minutes	5 minutes	5 minutes	20 hours

* Breathing stopped at end of half an hour. Heart continued to beat for eight hours.

The Condition of the Brain.

In the case of puncture of chest, followed by death five days later, which I mentioned in my second lecture, vascularity of the brain was noted as a special feature; there were a few small superficial hæmorrhages in the pia mater, and the

vessels over both hemispheres were much injected. On section the white matter had a pinkish colour, and there were numerous red spots where vessels had been cut across. The lateral ventricles contained no excess of fluid, and the vessels at the base and in the Sylvian fissures were healthy.

It is of course necessary to be very guarded, lest too great importance be attached to the degree of vascularity of a brain as observed on the post-mortem table, inasmuch as the position of the head is of importance in the distribution of the blood. It is also to be borne in mind that owing to inadequacy of valves in the jugular vein blood is readily forced upwards to the brain during convulsive seizures. Further, Mott,* in describing the condition of the brain in animals in whom the cerebral arteries had been ligatured, states that "in most of these brains experimented on a striking naked-eye feature was the distension of the veins of the cortex with blood, and frequently there was sub-pial hæmorrhage."

In the other case of puncture of lung with death in three days, the dura mater was described as being slightly thickened but without morbid adhesions, and the pia mater as slightly opaque; the vessels at the base were healthy, the brain tissue was fairly firm, and no obvious lesion could be detected in any part. In Cayley's case no naked-

* "Croonian Lectures," Lecture II, 'Lancet,' June 30th, 1900.

eye changes were found in the brain. Portions of the medulla were examined microscopically, and nothing abnormal was discovered; but this was in 1877, before the perfection of histological methods. In Goodhart's case no naked-eye changes were found in the brain.

In these cases, then, there was no evidence of gross lesion, and the cause of the non-recovery of the cerebral functions must be sought in some change affecting the nutrition of the neurone. Mott has described changes in animals after experimental ligature of the cerebral arteries, and doubtless similar changes would occur in man. In the animals, however, the vessels were permanently ligatured, and any return of blood-flow would depend on the establishment of a collateral circulation. Mott noted in addition to alterations in the cells and increase of blood in the superficial veins, an increase of fluid in the perivascular lymphatics and general œdema of the brain, which he took to be proportional and compensatory to the diminution of the arterial blood. This he ascribed to the establishment of a collateral circulation to the medulla and a concomitant secretion of an excess of cerebro-spinal fluid from the choroid plexus, which "would account for the œdema of the brain, the dropsical condition of the cells and the dilatation of the perivascular lymphatics."

It is possible that œdema of the brain may, however, occur in some of the clinical cases as

suggested by Raynaud's observation on his second case—vision was obscured and the right papilla was surrounded by serous effusion, the veins were in some places much swollen and in others compressed and empty—and by Lorey's case, in which the retinal arteries were much reduced in calibre and the veins in part dilated. Further, Leonard Hill* noted and figured the condition of the fundus in a dog in which he had tied the two carotids and the vertebrals. The veins were very large and the arteries exceedingly small; the disc was pale but not swollen. These observations suggest the presence of an increased intra-cranial tension such as would be produced by œdema of the brain, and are sufficiently striking to suggest the trial of the withdrawal of cerebro-spinal fluid by lumbar puncture in any future cases of this kind.

Convulsive seizures are a noticeable feature in these cases and would raise the intra-cranial pressure—a condition probably favourable to the passage of blood from the cerebral capillaries into the perivascular spaces.

Until further knowledge of the histological changes in the brain in these cases is forthcoming, the cause of the non-recovery must be attributed to injury to the neurons and possibly to cerebral œdema.

Review of the Symptoms.

The cases come under very different categories:

* 'The Cerebral Circulation,' 1896, p. 140.

first, sudden cardiac inhibition during puncture of chest or lavage of pleura ; secondly, cardiac inhibition in patients already unconscious from the influence of chloroform ; and thirdly, experiments on animals in which no cardiac inhibition occurs, the supply of blood to the brain alone being abolished.

In the first group the inhibition may be of varying degrees of intensity and duration :

(*a*) Sudden severe fatal syncope. Numerous cases as noted are on record.

(*b*) Sudden syncope followed by complete recovery after the most alarming symptoms, as in the cases recorded by Armstrong, Raynaud and Lorey. Suddenness of onset is very characteristic ; there is absolutely no warning of the onset of trouble. The appearance is either that of sudden death with total disappearance of pulse, arrest of respiration and pallor of face, sometimes with transient rigidity of limbs, or short of that there is sudden unconsciousness, gasping respiration, dilatation of pupils, extreme feebleness of pulse, and cyanosis.

In one of Raynaud's cases the patient was completely unconscious for a quarter of an hour with involuntary micturition and defæcation : this state was followed for three quarters of an hour by stertorous breathing, and when consciousness was regained paralysis of the right arm was observed. Recovery took place in a few days. In Ramsay's case of resuscitation after chloroform syncope

the patient was delirious before recovery took place. In Raynaud's second case there were convulsive movements of arms and recovery followed in half an hour. A second pleural lavage on the same day was followed by coma of several hours' duration succeeded by death after a series of fits. In Lorey's case the same alarming symptoms occurred and death also followed a second lavage—a strong warning of the risk attending a second interference with the lung or pleura in cases presenting such signs as cardiac shock.

(*c*) Sudden syncope; partial recovery, followed by death after varying periods of time.

This group may be compared with the cases occurring under chloroform anæsthesia in which the onset of symptoms is denoted by arrest of pulse and respiration, but with the resuscitation of the heart and with the disappearance of the effects of the anæsthetic these cases are identical save for the extra shock attending the surgical operation. They are also comparable to a considerable extent with the third group—the animals whose cerebral vessels were ligatured for varying times, save that in these the circulation through the rest of the body was maintained.

The onset.—The suddenness of onset is highly characteristic, and may be compared with the equally sudden onset of unconsciousness in the fit of idiopathic epilepsy.

Pulse.—This in some cases cannot be felt at the wrist, in others it has been noted as feeble or slow or intermittent.

Spasms: (a) *Initial tonic spasm.*—In the case of sudden death I reported tonic extensor spasm of arms was noted, with a convergent squint. In Cayley's case the patient's arms "stiffened." In Vallin's case rigidity of limbs was noted. This initial spasm is to be distinguished from the later convulsive movements, and would appear to be the direct result of the sudden cessation of the cerebral circulation. It probably occurs oftener than is recorded, as the extreme urgency of the cardiac failure in these cases is not conducive to observations of transient symptoms. In the cases of chloroform syncope the anæsthetic would doubtless negative the spasm. In the experiments on cats "there was usually a sudden stiffening of all the muscles following occlusion, with violent movements of fore and hind limbs and tail . . Then the fore-limb movements ceased; shortly afterwards the hind limbs relaxed, and the whole animal lay limp and quiet until after the restoration of the cerebral circulation." The sudden stiffening is obviously the same phenomenon as the initial tonic spasm in man, the violent movements of limbs and tail probably depending on the fact that the spinal circulation was intact in the animals. (Leonard Hill noted the frequency of extensor rigidity when the limit of cerebral anæmia is reached and the excitability of the cortex is vanishing.) This initial spasm is seen in the tonic spasm observed after the unconsciousness and fall of the epileptic fit.

(b) *Clonic convulsions.*—These do not seem to occur in the cases of sudden and permanent cardiac inhibition. In the two cases I have seen, in one, the child with sudden death, only extensor tonic spasm of arms was observed; in the other, which occurred when I was syringing out the pleural cavity, the patient, who was sitting up in bed, fell backwards with absolute suddenness. There certainly were no clonic convulsions, and I do not remember whether any tonic spasm occurred.

Clonic convulsions in these cases appear to be conditioned by the return of the cerebral circulation. Their time of onset varies very considerably. They may appear very soon after the onset of syncope. In one of Raynaud's cases they occurred at the end of a minute, and in others they seem to have appeared very quickly, though exact observations of their time of appearance are naturally scanty. Or they may appear much later, as in the case of the child at St. Thomas's Hospital, in whom the first fit occurred two hours after the attack. Considerable variation was also noticed in the experiments on cats, in whom the convulsions might appear speedily after the release of the vessels from occlusion, or not for an hour or more. With a very long period of complete cerebral anæmia the functions of the cortex and tracts must be permanently abolished. With periods of anæmia shorter than this the excitability of the cortex and the conductivity of the tracts revive on restoration of the circulation.

Subsequent course of these cases.—In addition to the symptoms already mentioned the pupils dilate and become insensitive to light. Involuntary micturition and defæcation occur. Severe perspirations are common. Consciousness does not return, convulsions may recur from time to time, the deep reflexes may be exaggerated, irregular movements or rigidity of one limb or of both limbs of one side may occur, hemi-anæsthesia may be detectable, and finally death occurs. In one case here recorded death did not occur till the fifth day. In the case of the cats definite dementia was noted in some cases following long occlusion of vessels. A similar condition has been observed by Leonard Hill in dogs and monkeys. It is conceivable that in man periods of cerebral anæmia of slightly shorter duration than those producing death might produce the characteristic symptoms of sudden syncope followed by a convulsive period terminating in dementia instead of death.

These cases of sudden and prolonged failure of the cerebral circulation are of great importance, not merely in that the clinical symptoms are of profound interest, but in view of the gravity of these accidents. They have also, I think, some bearing on the phenomena of epilepsy. Following upon a sudden arrest of the circulation, sudden syncope with unconsciousness is produced. In several cases transient tonic spasm was observed, and it may be that this is a common symptom.

The first two symptoms of an epileptic fit are thus reproduced. Inasmuch as the arrest of the cerebral circulation in the cases just described was of very considerable duration, so long, in fact, as to render recovery impossible, the subsequent symptoms of necessity differ from those of the transient epileptic fit. Clonic convulsions do, however, occur with the return of the circulation. The condition bears some resemblance to status epilepticus and a stronger resemblance to some cases of uræmia. It is unquestionably the result of the severe cerebral anæmia, and in the next section evidence will be given that both status epilepticus and uræmic coma and convulsions also depend upon the same factor.

On Diminution in the Blood-Flow through the Brain as the Result of Increased Intra-Cranial Tension.

The experimental results following increased intra-cranial tension have been studied by Harvey Cushing.* He increased intra-cranial tension in dogs by suitable means, and he showed that, if the intra-cranial pressure be rapidly increased, "Kussmaul-Tenner spasms, evacuation of bladder and rectum, practical cessation of respiration, and pronounced vagus effect upon the heart, often with

* "Some Experimental and Clinical Observations concerning States of Increased Intra-cranial Tension," 'Amer. Journ. of the Med. Sciences,' 1902, cxxiv, p. 375.

a complete standstill, lasting from ten to twenty seconds, may develop. Then follows a release from this extreme vagus inhibition, and the vaso-motor centre exerts its influence." With a slower increase of the intra-cranial pressure a different series of events occurred. The pressure against the brain could be increased to the point of its equalling the blood-pressure before any symptoms referable to the centres in the medulla were called forth. Direct examination of the cortex through a circular disc of glass fitting tightly into a second trephine hole showed, at this period of equalisation of blood-pressure and intra-cranial tension, an abrupt blanching of the exposed convolutions. The pulsating arteries could be seen against the blanched background and the dark blue veins in the sulci remained filled with blood, but presumably little, if any, circulation passed between them. The usual consequence was not death but a stimulation of the vaso-motor centre, which occasioned a rise in blood-pressure sufficient to overcome the high intra-cranial tension; the cerebral circulation was re-established, and the rosy colour could be seen through the glass window in the trephine hole to return again to the blanched convolution. With further increase in intra-cranial tension the blood-pressure rose *pari passu*, and always to a point exceeding the intra-cranial tension. This process could be repeated until the arterial pressure was forced to two or three times its normal level, sometimes to as much as

250 mm. Hg., without evidence of vaso-motor failure. In face of these experiments, Cushing's conclusion that increased intra-cranial tension occasions a rise of blood-pressure, which tends to find a level slightly above that of the pressure exerted against the medulla, seems absolutely justified. By this mechanism the vital centres in the medulla and the life of the brain and entire animal are protected.

Clinically it is well established that many of the symptoms of cerebral tumour, hydrocephalus, cerebral hæmorrhage, etc., are dependent upon an increase of the intra-cranial vision. Among such symptoms may be mentioned headache, vomiting, coma, convulsions, choked disc, etc. Extraordinary relief to these symptoms is attained after the pressure is relieved by surgical intervention. An admirable series of cases has been recorded by Harvey Cushing.*

In another paper Cushing† gives the records of five cases of intra-cranial hæmorrhage, four traumatic and one apoplectic. These illustrate, from the clinical standpoint, the facts ascertained by him experimentally.

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* "The Establishment of Cerebral Hernia as a Decompressive Measure for Inaccessible Brain Tumours,' 'Surgery, Gynæcology, and Obstetrics,' 1905, i, pp. 297–314.

† "The Blood-pressure Reaction of Acute Cerebral Compression illustrated by Cases of Intra-cranial Hæmorrhage," 'Amer. Journ. of the Med. Sciences,' 1903, cxxv p. 1017.

In one case of apoplectic cerebral hæmorrhage the blood-pressure before operation registered 300 mm. Hg., whilst after trephining and the evacuation of blood it began to fall at once, and in twenty minutes had reached the normal.

The clinical evidence as obtained, therefore, from cases of cerebral tumour, cerebral hæmorrhage, etc., is in complete accord with the conclusions arrived at experimentally by Harvey Cushing. To recapitulate, it is clear that a rise in intra-cranial tension produced by the introduction of any foreign element, such as a tumour mass, blood, etc., must tend to diminish the blood-flow through the brain. As the tension increases, a point would be reached at which the intra-cranial tension equals that of the general blood-pressure. The cerebral circulation would therefore cease, were it not that by a compensatory process the general blood-pressure rises to a point above that of the intra-cranial pressure, and thereby maintains the flow of blood through the brain. But with a great increase of intra-cranial tension certain general effects are produced, apart from focal symptoms, dependent upon the position of the lesion. Headache, for instance, is common, and is probably attributable to tension of dura mater and tentorial structures.

Optic neuritis is to be attributed, in the main, to a passive venous congestion of the retinal veins, and subsides or improves on relief of intra-cranial tension, sometimes with extraordinary rapidity.

Finally, coma is almost invariable in the last

stages of cerebral tumour, and in large cerebral hæmorrhages. Convulsions are also frequent in these conditions. Both are remarkably improved by methods capable of lowering the cerebral pressure, such as trephining or lumbar puncture. And it is to be noted that, by lowering the intra-cranial tension, a free access of blood to the brain is facilitated.

Uræmia.

Uræmic convulsions may be absolutely indistinguishable from those of idiopathic epilepsy, and if it can be shown that there is evidence of a condition of cerebral anæmia in uræmia, support would be lent to the similar theory as applied to epilepsy. In a paper read before the West London Medico-Chirurgical Society I brought forward evidence to show that the cerebral manifestations of uræmia are due to cerebral anæmia produced by an increase of intra-cranial tension, resulting in all probability from cerebral œdema.*

In cerebral uræmia we frequently see a symptom-complex almost identical with that of cerebral compression, viz. headache, vomiting, drowsiness, coma, convulsions, optic neuritis, etc. This symptom-complex is, at any rate in great measure, dependent upon increased intra-cranial tension; for many cases are now on record in which extraordinary relief has followed lumbar puncture,

* "Uræmia," 'West London Medical Journal,' 1907, xii, p. 9.

a procedure which, by means of allowing some of the fluid to escape, diminishes the pressure within the cerebro-spinal space. Numerous cases of uræmia were quoted from the literature in which marked relief had followed on the lowering of intra-cranial tension by means of removal of cerebro-spinal fluid by lumbar puncture. I will only quote here Willson's cases as a type. In two papers he records ten cases.* Of the ten cases, six had convulsive movements, general in five and unilateral in one. In every case the convulsions terminated on the withdrawal of the cerebro-spinal fluid, and in only one did they return within several weeks of the operation. His best results were obtained in those cases in which the fluid spurted from the cannula, *i. e.* in which the pressure was greatest. In the autopsies of fatal cases (three out of the ten) increased cerebro-spinal fluid, dilated ventricles, and œdema of the brain were found. A sufficient number of cases were quoted to show that marked relief may follow lumbar puncture in cases of uræmia. It is well known that uræmic convulsions and coma may disappear apart from such treatment, but the promptitude with which the improvement occurred was such

* Willson, "The Pathogenesis of Uræmia and Eclampsia," 'Journ. of Amer. Med. Assoc.,' 1904, p. 1019; also "The Relief of Uræmic Hemiplegia and other Uræmic States by Lowering Intra-cranial Pressure," 'Transactions of College of Physicians of Philadelphia,' 1905, xxvii, p. 34.

as to leave no doubt in the minds of the observers that the relation was one of cause and effect. It is noteworthy also that in most of the cases the cerebro-spinal fluid did escape under considerable pressure.

The cerebro-spinal space is a practically closed-in cavity, with walls of considerable rigidity. This cavity is always full of fluid or semi-fluid substance, and to force more fluid into such a space would necessitate great pressure, were it not that by compression of blood-vessels the volume of blood contained in the cranium can be diminished. But after a certain point the peripheral blood-pressure rises, and further accumulation of fluid would meet with rapidly increasing resistance, and a small additional quantity would materially raise the cerebro-spinal pressure ; *vice versa*, the removal of a very small quantity could materially lower it.

But relief has not always attended the performance of lumbar puncture in uræmia, and this may be due to the fact that this operation can only relieve intra-cranial pressure by removal of the *free* cerebro-spinal fluid. If, however, the pressure is mainly produced by a cerebral œdema, then, unless a co-existent excess of free ventricular fluid was present, the removal of the little that would flow might not be sufficient to relieve the pressure materially.

The manifestations of uræmia here considered, which are so strikingly relieved by lumbar puncture, are, as has been pointed out, closely similar to the

pressure symptoms produced in other conditions, such as cerebral tumour and cerebral hæmorrhage, and the fact that the cerebro-spinal fluid is often under considerable pressure in these cases of uræmia indicates that the underlying condition of increased intracranial tension must be responsible for the symptoms.

Harvey Cushing, indeed, makes this suggestion in the paper on the establishment of cerebral hernia above referred to: "I have come to believe that the same causes must underlie the choked disc of tumour and the so-called retinitis associated with renal disease. It seems not improbable that an increase of intra-cranial tension due to cerebral œdema may be responsible for the occasional retinal changes in Bright's disease, as well as for the headache and vomiting which may characterise it."

The correctness of Cushing's views, founded on a series of brilliant researches, both experimental and clinical, are still further supported by a recent account of a case of uræmia in which sub-temporal decompression was attended with must successful results.*

The patient was a woman, æt. 22 years, with œdema, headache, and vomiting. Both discs were swollen. Right 6 D., left 7 D. The discs were very

* Harvey Cushing and James Bordley, jun., "Subtemporal Decompression in a Case of Chronic Nephritis with Uræmia, with Special Consideration of the Neuroretinal Lesion," 'Amer. Journ. of Med. Sci.,' October, 1908.

œdematous, the physiological cup was filled in, and there were many retinal hæmorrhages. Vision failed rapidly. Later the retinæ were so swollen that it was impossible to locate the discs. The retinæ were covered with hæmorrhages and yellowish-white patches of exudation, and the arteries were invisible. Lumbar puncture gave no relief. Right subtemporal decompression was performed. The dural veins were considerably congested, the arteries markedly tortuous and sclerotic. The subdural space contained no free fluid. The arachnoid was *markedly distended with fluid*, which escaped after pricking the membrane in spaces where it bridged over the sulci. The brain itself appeared "soggy and wet." The headache subsided, stupor rapidly disappeared, and the patient's lethargic state was replaced by one of normal mental activity.

Eleven days later the swelling of the discs did not exceed 1 D., and the retinal tissue was much clearer, and still further improvement had occurred by the time she left hospital. She was admitted a month later, stuporous and with Cheyne-Stokes' breathing. Death was due to cerebral hæmorrhage, and the kidneys were small and granular.

The authors' conclusions were that the neuro-retinal and cerebral manifestations of uræmia are due to œdema of the brain.

Uræmic coma.—The foregoing facts indicate that in uræmia a state of increased intra-cranial

tension is present, and that relief of tension by lumbar puncture or decompression causes a marked alleviation of the symptoms. Traube's view that cerebral œdema (which would produce the rise in the intra-cranial tension) is the cause of anæmia is strongly supported by the above facts, and especially by the striking case of decompression.

The late Dr. Beevor also remarked when injecting brains of people dead from various causes, that "it was particularly observed that the cases, where the injection did not penetrate well were those suffering from granular nephritis or alcoholism, where there was much fluid in the subarachnoid space of the brain." *

Concurrently with the increase of intra-cranial tension the blood-pressure rises, and we see the slow, tense pulse so common in uræmia. This conservative rise of blood-pressure maintains the cerebral circulation. If the tension progressively rises the compensatory rise of blood-pressure cannot go on indefinitely, and a point may be reached beyond which no amount of vaso-constriction and cardiac augmentation can maintain an adequate cerebral circulation. If this point is reached gradually and the volume of blood passing through the brain be slowly diminished, we should expect a comatose condition to develop, the last stage of cerebral compression with gradual

* C. E. Beevor, "On the Distribution of the Different Arteries Supplying the Human Brain," 'Royal Soc. Phil. Trans.,' 1908, series B, vol. cc, p. 15.

respiratory failure, the high-tension slow pulse of the early stage of compression changing into a soft, rapid pulse, with the developing vaso-motor failure. A concomitant toxic action on the brain is not denied; such may be present and aid in the production of the cerebral symptoms. But the anæmia alone should suffice to induce the coma.

Uræmic convulsions.—Under the severe strain imposed upon the heart in working against this conservative high blood-pressure it may fail rapidly in chronic nephritis. Should this occur, or should the vaso-motor centre fail rapidly, it is clear that the cerebral circulation must fail equally rapidly when the intra-cranial tension is pathologically high. Instead of headache and somnolence, gradually developing into coma, a more sudden unconsciousness would result, and convulsions would readily be produced.

According to Strumpell,* "the pulse is often very slow before the appearance of severe symptoms, sometimes 48 or 40, but it is almost always tense and hard. In chronic uræmia also a moderate slowness of the pulse is not infrequent. When uræmic convulsions appear, however, the pulse usually becomes small and very frequent, especially in cases that terminate unfavourably."

Willson's cases above recorded are of the greatest

* Strumpell, 'Text-book of Medicine,' third American edition, p. 600.

importance in this connection, especially as, in his six cases of uræmic convulsions, the convulsions terminated in every case on the withdrawal of the cerebro-spinal fluid; and it is to be noted that his best results were obtained in those cases in which the fluid spurted from the cannula, *i. e.* in which the pressure within the cerebro-spinal space was greatest. And this withdrawal of fluid, by lowering the cerebral pressure, would allow of an immediate return of blood to the brain.

In cases of acute uræmia in acute nephritis it is well known that an increase of blood-pressure is common, and the cardiac failure may be more readily induced owing to the more toxic character of some of the diseases associated with acute nephritis, the poisons of the acute infections, such as scarlet fever, materially affecting the heart muscle. The heart would thereby be unable to respond to the vaso-constriction above described, and the conservative rise of blood-pressure would fail more rapidly.

In conclusion, it is submitted that the pathology of the cerebral manifestations of uræmia is to be sought in a condition of œdema and increased intra-cranial tension with failure of the cerebral circulation produced in the manner suggested, a gradual failure producing coma, a rapid one, convulsions.

If this conclusion be correct, strong support is lent to the theory that the fits of idiopathic epilepsy are produced by sudden failures in the

cerebral circulation, for it is notorious that the convulsions of uræmia and of idiopathic epilepsy may be absolutely indistinguishable, and it is extremely probable that the factor underlying conditions so remarkable and so identical should be one and the same.

The local palsies of uræmia.—In addition to the headache, convulsions and coma of uræmia local palsies may occur, such as hemiplegia, monoplegia, aphasia, amaurosis, etc. These are often only temporary and must therefore be due to some factor which may appear, last for a variable time, and then disappear. Two possible factors at once suggest themselves—arterial spasm and localised cerebral œdema. Both have been suggested as possible explanations of these local and transient symptoms of uræmia.

The question of cerebral vaso-motor spasm has been discussed in a previous lecture, and such spasm has been brought forward by various observers as a possible explanation of the transient paralyses of arterio-sclerosis. I think that some of these latter, especially those noted on awaking from sleep, may depend on a passing depression of the blood-pressure diminishing the blood-flow through a diseased and narrowed artery to a point below that essential for adequate nutrition of the related area of brain tissue.

Local œdema of the brain would be equally efficacious in arresting or diminishing the blood supply, and Cushing and Bordley noted in their

case that "the arachnoid was markedly distended with fluid which escaped after pricking the membrane in spaces where it bridged over the sulci. The brain itself appeared soggy and wet."

Collateral evidence of the occurrence of localised cerebral œdema may be found in a case published by Professor Osler.

"The patient was a medical man æt. 29 years. At the age of twelve he had an attack of right hemiplegia and aphasia which lasted for a week or ten days. Within the year he had five or six further attacks of hemiplegia, each successive one less severe and not accompanied by aphasia, and from that date was subject to occasional attacks of numb, tingling sensation in the side. From the age of twenty-six he became subject to severe attacks of migraine. At twenty-eight he had a sudden attack of swelling and pain in the feet, and at the same time he began to suffer from soreness at the ends of the fingers. He had frequent attacks of angio-neurotic œdema of the upper lip and outbreaks of urticaria associated with severe darting pains in the legs. He had one attack of abdominal colic with pains in the calves of the legs and an outbreak of purpura and urticaria; later he suffered from hæmaturia and albuminuria. Professor Osler considered that the recurring attacks of hemiplegia were probably associated with changes in the brain of essentially the same nature as those which subsequently occurred in the lip and skin—in other words that an angio-neurotic œdema occurred in

the brain substance, and it is difficult to see how this conclusion can be avoided.

I quote this case in detail because it does give support to the view that local œdema can occur in the brain and can give rise to local paralyses. Inasmuch as these paralyses are so frequently transient the direct evidence of the post-mortem table is not available.

Cushing and Bordley, as the result of their observations on their cases of cerebral decompression, came to the conclusion that the local and transient hemiplegias, aphasias, amauroses and Jacksonian fits of uræmia, were also due to œdema of the brain.

Status Epilepticus.

Morgan Hodskins and Arthur Morton* have reported a series of seven cases of status epilepticus treated by lumbar puncture. As they are of considerable importance I give them in some detail.

"Case 1.—March 26th, 1904: After forty fits (at intervals of about fifteen minutes) lumbar puncture was performed; 12 c.c. of fluid withdrawn, not under very high pressure. Convulsions ceased for over two hours, then recurred, thirty-five in the next two days, but not so severe. Then slow recovery.

"Case 2.—April 18th, 1904: Status epilepticus. One hundred grains of sodium bromide given

* "Lumbar Puncture in Status Epilepticus," 'Boston Med. and Surg. Journ.,' 1905, clii, p. 700.

hypodermically with no effect. Lumbar puncture after twenty-four severe fits, and 14 c.c. fluid withdrawn under increased pressure. Only one more fit in next twelve hours, then a few slight ones, easily controlled, followed by exhaustion, paralysis of pharynx and extremities. Slow recovery.

"Case 3.—April 18th, 1904: Twenty-five fits. Lumbar puncture, and removal of 14 c.c. of fluid under slightly increased pressure. Five slight fits in next two and a half hours, then cessation of fits and quick recovery.

"Case 4.—May 19th, 1904: Twenty-five fits. Lumbar puncture; withdrawal of 14 c.c., not under greatly increased pressure, until convulsions occurred, when it squirted out in a stream. No effect; seventy-five fits in twenty-four hours, and death on following day.

"Case 5.—August 29th, 1904: Seventy-five to one hundred fits daily for past three days. Lumbar puncture and withdrawal of 15 c.c. under considerable pressure. Free from fits for three and a half hours, then a recurrence, the temperature rising to 109° F. before death.

"Case 6.—Status epilepticus. September 12th, 1904: Status for thirty-six hours. Lumbar puncture; 15 c.c. of fluid withdrawn under increased pressure. Free from fits for eight hours; then return of fits. Rise of temperature to 107° F. Death.

"Case 7.—Status epilepticus. October 12th, 1904: Twenty-five fits. Lumbar puncture; 20 c.c.

of fluid withdrawn under increased pressure, followed by injection of 10 c.c. of sodium bromide solution (gr. xxx to the ounce). One fit occurred in the next fifteen hours. Slow recovery. The blood-pressure, which before the puncture measured 140 mm. of mercury, fell to 127 mm. afterwards."

In another case reported by R. C. Allen * lumbar puncture was performed at the end of prolonged status when death appeared imminent. The cerebro-spinal fluid spurted out under considerable pressure; three ounces were allowed to escape. The fits ceased and improvement was immediate. The pulse, which was barely perceptible, became stronger. Consciousness returned in twelve hours, the patient was torpid and lethargic for six days, and then became perfectly well.

It is noteworthy that in five out of the eight cases recovery ensued, and that in every case but one there was an immediate and marked improvement as the result of the lumbar puncture. Further, in seven of the cases the cerebro-spinal fluid was evidently under increased pressure, and in the only case in which the blood-pressure was estimated it fell from 140 mm. of mercury to 127 mm. as the result of the puncture. These facts suggest that the condition of status is similar to what is seen in uræmia, in which, as has been pointed out, there is an increase of the cerebro-spinal pressure. And this increased pressure

* 'Brit. Med. Journ.,' April 11th, 1908, p. 865.

would tend to produce an anæmia of the brain unless the blood-pressure rose to a point higher than that obtaining within the cranial cavity. The inference, therefore, that status epilepticus is due to anæmia of the brain brought about by increased intra-cranial tension does not appear unreasonable. It is possible that an unduly severe and prolonged fit in some way evokes œdema of the brain, and that the increased pressure resulting from this is responsible for the anæmia and the continuance of the fits.

Mott* has shown that "the essential changes in the brain in cases of status epilepticus are :—

"(1) Great venous congestion and stasis.

"(2) *Œdema of the brain* and marked distension of the perivascular lymphatics, flattening of the convolutions and naked-eye increased vascularity ; but inasmuch as the brain is contained in a closed cavity, venous stasis and œdema must be associated with a corresponding *arterio-capillary anæmia.*"

It is interesting also to note that Mott finds that experimental ligature of arteries in animals leads not only to anæmia of the brain, but also to œdema. Continuing the above quotation :

"In the case of experimental ligation of arteries in animals the effect may be similar, but it is

* "Preliminary Communication upon the Changes in the Brain, Spinal Cord, Muscles, and other Organs, found in Persons Dying after Prolonged Epileptiform Convulsions," 'Archives of Neurology,' London, i, p. 499.

brought about by an entirely converse process; the œdema of the brain and venous stasis are here proportional to, and determined by, the diminution of arterial blood in the arterio-capillary systems. . . . Microscopical observations show that the whole brain is permeated by a canalicular lymph system containing cerebro-spinal fluid, the large processes of the neurons lying in lymph spaces which are continuous with the perivascular lymphatics. These perineuronal spaces were very obvious in some of the cases of experimental anæmia."

In this connection it is a striking fact that, in his description of the photo-micrographs accompanying his paper, Mott comments on the close similarity between the appearance of the brain-cells and perineuronal spaces in experimental anæmia of the brain (by ligature) and in status epilepticus.

These observations, both clinical and pathological, lead to the conclusion that the fundamental condition underlying the condition of status epilepticus is cerebral œdema and anæmia. It might be urged that, inasmuch as it is not probable that there is a great rise of cerebral pressure, the heart should be able to respond by more powerful contractions which would maintain the cerebral circulation (*vide* Harvey Cushing's observations). It is interesting to note in this connection that the heart in cases of status epilepticus shows extreme fatty degeneration;

thus Mott* has shown that "the œdema of the muscle substance of the heart is very striking upon microscopical examination; networks of capillaries are seen, small hæmorrhages are sometimes observed, and the fibres are separated from one another by a serous exudation. This of itself would embarrass the much over-worked organ; but the lymph around the muscle-fibres no longer constitutes a normal environment; it contains excess of carbonic acid, deficient oxygen, and toxic fatigue products, the result of excessive muscular activity and imperfect metabolism. The fibres, thus imperfectly nourished and oxygenated, are the seat of an imperfect metabolism which is manifested upon microscopical examination by a lustreless appearance, indistinctness of striation and accumulation of minute particles of fat in the substance of the fibres. . . . In seven cases of status epilepticus, and in a large number of cases of general paralysis dying after prolonged convulsive seizures, I have invariably found this fatty change in the heart and striated muscles."

The Epileptiform Seizures of General Paralysis.

Mott has shown that "œdema of the brain, owing to dilatation of the perivascular lymphatics, is a striking feature in general paralysis, and the water which can be extracted from the brain by

* Mott, *loc. cit.*, pp. 502, 503.

placing it in a desiccator is larger in amount than in the normal brain. But venous congestion and œdema of the brain must be associated with arterial anæmia. . . . If all the arteries to a dog's brain be ligatured there is established an arterial anæmia, but the veins of the cortex will be found greatly congested, the perivascular lymphatics distended, and the motor cortex excitable, even hyper-excitable, to electric stimulation. This makes it probable that the epileptiform seizures of general paralysis are associated with and probably dependent upon venous congestions and stasis, arterial anæmia and increased excitability."

Conclusions.

In these lectures it has only been possible to touch upon certain aspects of a very large and difficult subject. It has been my purpose to endeavour to show that variations in the cerebral circulation, apart from gross lesions such as hæmorrhage, thrombosis, and embolism, exercise a very great influence in the production of nervous symptoms. Such variations in the cerebral circulation are often associated with equally marked variations in the peripheral circulation and in the action of the heart. It has been submitted that alterations in the circulation afford an adequate explanation, not only of the ordinary fainting fit, but also of the more prolonged attacks characterised by cardiac, vasor-motor and cerebral symptoms. I have urged that these cases, which

in some respects are so closely allied to epilepsy, the suddenness of some faints and the conversion of faints into fits, afford strong evidence that the epileptic fit itself owes its origin to some disturbance of the circulation. Corroborative evidence is afforded by the accuracy with which the symptoms of the various stages of the epileptic fit are reproduced in cases of heart-block due to heart disease. Finally, evidence of the cessation of the heart's activity in epilepsy has been given. In the case of *petit mal* it has been suggested that two different factors may be concerned. In some cases the transient unconsciousness may be produced by a very transient cardiac failure; in others cerebral vaso-motor spasm may be concerned.

If these views are correct the pathology of epilepsy is carried only one stage further. The reason of these morbid cardio-vascular changes is yet to seek. A hereditary factor is obvious, and we must assume that there is an inherited instability of the sympathetic and cardio-vascular systems. The processes, both nervous and chemical, by which the cardio-vascular apparatus is governed are still far from clear; research in these directions may afford the clue to much that is at present obscure.

The serious symptoms produced by more prolonged cessation of the cerebral circulation have been considered.

Finally, the cerebral manifestations of uræmia have been discussed. It has been submitted that

these are simply due to increased intra-cranial tension with resultant interference with the cerebral circulation. Evidence has been given to show that this change is amply sufficient to account for all the manifestations of uræmia. It does not negative the importance of abnormal metabolic changes, which may have great influence in the production of other uræmic symptoms.

If I have seemed to dwell too fully on cases collected from the literature it is because such cases contain evidence of the views I have put forward, and as they have not been published with such intention, the evidence may be taken as quite unbiassed. Owing to the inherent difficulties before mentioned, viz. the evanescent character of many of these vascular changes and the fact that when they have subsided no organic change is left behind, this cumulative clinical evidence yields the chief clue to the nature of the processes we have been studying, pending the discovery of the real pathological change on which they depend.

ADLARD AND SON, IMPR., LONDON AND DORKING.